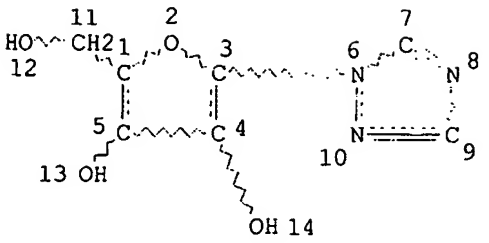
```
=> d his ful

     FILE 'REGISTRY' ENTERED AT 16:30:38 ON 19 MAY 2004
L29             STR
L30           0 SEA SSS SAM L29
L31           1 SEA SSS FUL L29

     FILE 'HCAPLUS' ENTERED AT 16:39:28 ON 19 MAY 2004
L32           1 SEA ABB=ON  L31

     FILE 'REGISTRY' ENTERED AT 16:40:14 ON 19 MAY 2004
L33             STR L29
L34           0 SEA SSS SAM L33
L35           1 SEA SSS FUL L33
                E RIBOFURANOSE/CN
L36             STR L33
L37           6 SEA SSS SAM L36
L38         127 SEA SSS FUL L36

     FILE 'HCAPLUS' ENTERED AT 16:42:38 ON 19 MAY 2004
L39        1951 SEA ABB=ON  L38
L40           1 SEA ABB=ON  L39 AND ?INFLAM?(W)?BOWEL?
L41           6 SEA ABB=ON  L39 AND (?INFLAM?(W)(?BOWEL? OR ?CROHN?) OR
                ?ULCER?(W)?COLITIS?)
```

127 compds from Registry - see 6 one-letter for structure

6 cits from CA Plus all include 1-β-D-ribofuranosyl-1-H-1,2,4-triazole-3-carboxamide — Claim 3.

```
=> d que stat l41
L36                 STR
```




```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L38          127 SEA FILE=REGISTRY SSS FUL L36
L39         1951 SEA FILE=HCAPLUS ABB=ON  L38
L41            6 SEA FILE=HCAPLUS ABB=ON  L39 AND (?INFLAM?(W)(?BOWEL? OR
                 ?CROHN?) OR ?ULCER?(W)?COLITIS?)
```

=> d ibib abs hitstr 141 1-6

L41 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:331903 HCAPLUS
DOCUMENT NUMBER: 140:337930
TITLE: Anti-CD20 antibody-drug conjugates for the treatment of cancer and immune disorders in mammal and human
INVENTOR(S): Wahl, Alan F.; Senter, Peter D.; Law, Che-leung; Cerveny, Charles G.
PATENT ASSIGNEE(S): Seattle Genetics, Inc., USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032828	A2	20040422	WO 2003-US23895	20030730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

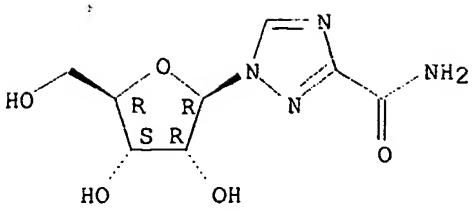
PRIORITY APPLN. INFO.: US 2002-400404P P 20020731

AB The present invention relates to methods and compns. for the treatment of CD20-expressing cancers and immune disorders involving CD20-expressing cells. The present methods comprise administering to a subject an anti CD20 antibody-drug conjugate that has a high potency and/or is capable of internalizing into CD20-expressing cells. The present invention further provides pharmaceutical compns. and kits comprising such conjugates. The present invention yet further provides methods of and compns. relating to combination therapy of cancer and immune disorders involving CD20-expressing cells using the anti-CD20 antibody-drug conjugates of the invention.

IT **36791-04-5D**, Ribavarin, conjugates with anti-CD20 antibody
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-CD20 antibody-drug conjugates for the treatment of cancer and immune disorders in mammal and human)

RN 36791-04-5 HCAPLUS
CN 1H-1,2,4-Triazole-3-carboxamide, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:301196 HCAPLUS
DOCUMENT NUMBER: 138:297636
TITLE: Use of STAT-6 inhibitors as therapeutic agents
INVENTOR(S): Carson, Dennis A.; Cottam, Howard B.; Leoni, Lorenzo M.; Barchechath, Sylvie
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031587	A2	20030417	WO 2002-US32503	20021009
WO 2003031587	A3	20040219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003143199	A1	20030731	US 2002-269110	20021009
PRIORITY APPLN. INFO.:			US 2001-328162P	P 20011009
			US 2001-328689P	P 20011010

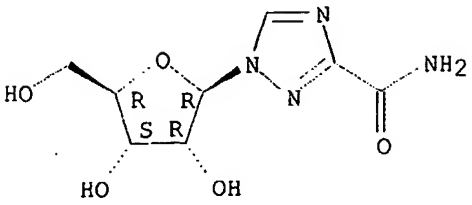
OTHER SOURCE(S): MARPAT 138:297636

AB The invention provides therapeutic method to enhance the efficacy of interferon treatment comprising administering to a mammal subject to interferon treatment a compound which is an antagonist of the IL-4 or IL-13 signal transduction pathway in an amount effective to enhance said efficacy. The method includes treatment of diseases such as cancer, proliferative fibrotic diseases, viral diseases, or autoimmune diseases. The invention also includes the use of chemotherapeutic agents, radiation or other treatments in conjunction with the method of the invention.

IT **36791-04-5**, Ribavirin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of STAT-6 inhibitors as therapeutic agents)

RN 36791-04-5 HCAPLUS
CN 1H-1,2,4-Triazole-3-carboxamide, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

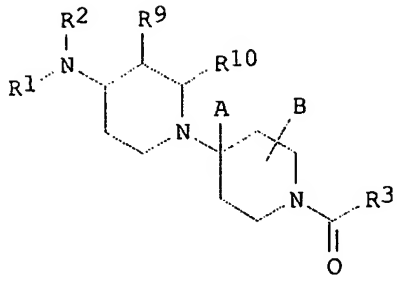
Absolute stereochemistry.



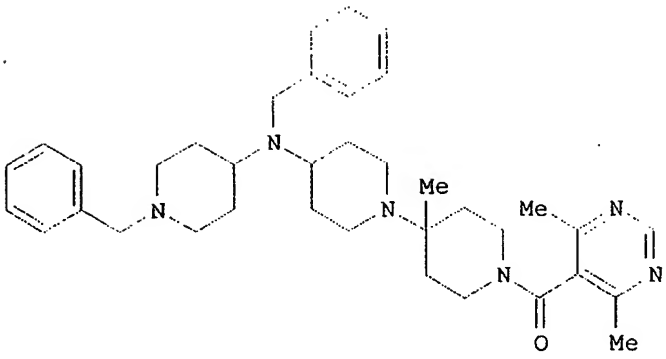
L41 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:202634 HCAPLUS
DOCUMENT NUMBER: 138:238191
TITLE: Preparation of 1-[1-(pyrimidin-5-ylcarbonyl)piperidin-4-yl]piperidin-4-amines as CCR5 antagonists
INVENTOR(S): Palani, Anandan; Miller, Michael W.; Scott, Jack D.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020716	A1	20030313	WO 2002-US27389	20020828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004010008	A1	20040115	US 2002-229466	20020828
US 2004092745	A1	20040513	US 2003-628933	20030729
US 2004092551	A1	20040513	US 2003-629466	20030729

PRIORITY APPLN. INFO.: US 2001-315683P P 20010829
US 2002-229466 A3 20020828
OTHER SOURCE(S): MARPAT 138:238191
GI



I



II

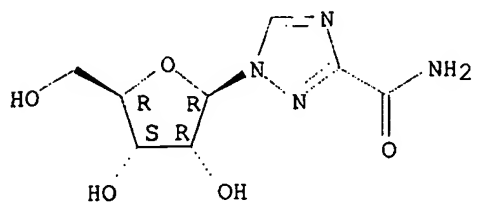
AB The title compds. [I; R1 = piperidinyl, Ph, etc.; R2 = CH2Ph, 4-pyridylmethyl, etc.; R3 = 4,6-dimethylpyrimidine-5-yl, Ph, etc.; R9, R10, B = H, alkyl, haloalkyl; A = H, alkyl, alkenyl] and their pharmaceutically acceptable salts, useful, alone or in combination with another agent, in the treatment of Human Immunodeficiency Virus (HIV), solid organ transplant rejection, graft v. host disease, arthritis, rheumatoid arthritis, **inflammatory bowel** disease, atopic dermatitis, psoriasis, asthma, allergies or multiple sclerosis, were prepared E.g., a 6-step synthesis of II, starting from 4-hydroxypiperidine and N-Boc-4-piperidone, which showed IC50 of 1.7 nM in luciferase HIV replication assay, was given.

IT **36791-04-5**, Ribavirin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 1-[1-(pyrimidin-5-ylcarbonyl)piperidin-4-yl]piperidin-4-amines as CCR5 antagonists)

RN 36791-04-5 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamide, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

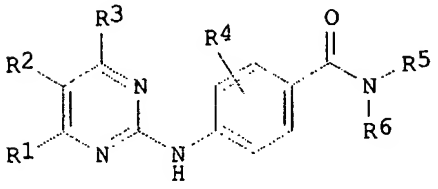
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:449662 HCAPLUS
DOCUMENT NUMBER: 137:33310
TITLE: Preparation of anilinopyrimidines as IKK inhibitors
INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046171	A2	20020613	WO 2001-US46403	20011205
WO 2002046171	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003203926	A1	20031030	US 2001-4642	20011204
AU 2002020195	A5	20020618	AU 2002-20195	20011205
EP 1349841	A2	20031008	EP 2001-999564	20011205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-251816P P 20001206
WO 2001-US46403 W 20011205

OTHER SOURCE(S): MARPAT 137:33310
GI



I

AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of ≤ 1 μM in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions

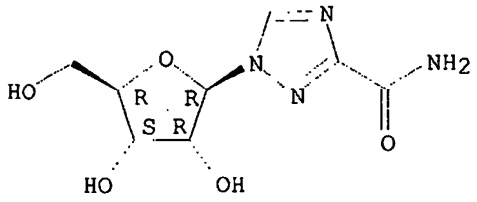
that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds.

IT **36791-04-5**, Ribavirin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agent; preparation of anilinopyrimidines as IKK inhibitors)

RN 36791-04-5 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamide, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:449661 HCAPLUS

DOCUMENT NUMBER: 137:33309

TITLE: Preparation of anilinopyrimidines as JNK pathway inhibitors

INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.

PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

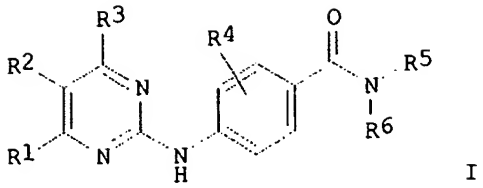
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046170	A2	20020613	WO 2001-US46402	20011205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003220330	A1	20031127	US 2001-4645	20011204
AU 2002027214	A5	20020618	AU 2002-27214	20011205
EP 1349840	A2	20031008	EP 2001-996103	20011205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-251904P P 20001206
WO 2001-US46402 W 20011205

OTHER SOURCE(S): MARPAT 137:33309

GI



I

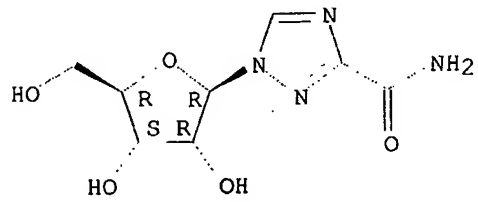
AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of the JNK pathway, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of ≤ 10 μM in the JNK2 assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to inhibition of the JNK pathway. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds.

IT **36791-04-5**, Ribavirin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agent; preparation of anilinopyrimidines as JNK pathway inhibitors)

RN 36791-04-5 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamide, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:635933 HCAPLUS

DOCUMENT NUMBER: 135:215973

TITLE: Use of peptide conjugates for enhancing drug delivery across biological membranes and tissues

INVENTOR(S): Rothbard, Jonathan B.; Wender, Paul A.

PATENT ASSIGNEE(S): Cellgate, Inc., USA

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062297	A1	20010830	WO 2001-US4459	20010209
WO 2001062297	C2	20030109		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002009491	A1	20020124	US 2001-779693	20010207
EP 1263469	A1	20021211	EP 2001-909135	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523982	T2	20030812	JP 2001-561360	20010209

PRIORITY APPLN. INFO.:

US 2000-182166P	P	20000214
US 2001-779693	A	20010207
WO 2001-US4459	W	20010209

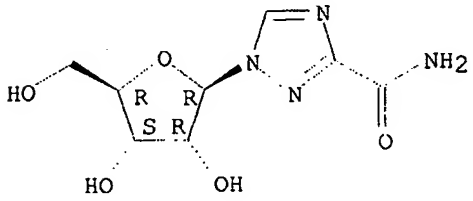
AB This invention provides compns. and methods for enhancing delivery of drugs and other agents across a biol. barrier, including epithelial tissues such as the skin, gastrointestinal tract, pulmonary epithelium, and the like. The compns. and methods are also useful for delivery across endothelial tissues, including the blood brain barrier. The compns. and methods employ a delivery enhancing transporter that has sufficient guanidino or amidino sidechain moieties to enhance delivery of a compound across one or more layers of the tissue, compared to the non-conjugated compound The delivery-enhancing polymers include, for example, poly-arginine mols. that are preferably between about 6 and 50 residues in length. Taxol conjugates with a heptamer of arginine was soluble in water in contrast with taxol itself. The conjugate was equally potent when assayed for biol. activity using standard cytotoxicity assay.

IT **36791-04-5**, Ribavirin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of peptide conjugates for enhancing drug delivery across biol. membranes and tissues)

RN 36791-04-5 HCAPLUS

CN 1H-1,2,4-Triazole-3-carboxamidé, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs ind hitstr 128 1-15

L28 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:775951 HCAPLUS
DOCUMENT NUMBER: 134:80763
TITLE: Effect of opioid-active therapeutics on the ascending reflex pathway in the rat ileum
AUTHOR(S): Allescher, H. D.; Storr, M.; Piller, C.; **Brantl, V.**; Schusdziarra, V.
CORPORATE SOURCE: Department of Internal Medicine II, Technical University of Munich, Munich, 81675, Germany
SOURCE: Neuropeptides (Edinburgh) (2000), 34(3&4), 181-186
CODEN: NRPPDD; ISSN: 0143-4179
PUBLISHER: Harcourt Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For a long time therapeutic agents that interact with opioid receptors have been used in antidiarrheal therapy. The action of the opioid active substances on motility and transit have already been characterized; however, their effects on myenteric reflexes and their possible luminal action have not yet been investigated. Loperamide, fedotozine and β-casomorphin-4, as well as the casomorphin-analog β-CM-4027, are, or have been, suggested as therapeutic agents and were studied in the isolated rat ileum for their effect on the ascending reflex pathway. β-CM-4027 > fedotozine > loperamide > β-casomorphin-4 caused a concentration-dependent inhibition of the ascending contractile reflex response with an IC50 of 1.4+10-7M, 1.5+10-6M, 4.1+10-6M and 4.5+10-6M resp. At the same time as the oral contractile reflex response was inhibited, all four opioid agonists (CM-4027 > β-casomorphin-4 > fedotozine > loperamide) increased the latency of the reflex response. Both effects were blocked by naloxone, indicating the involvement of opioid receptors. These results demonstrate that opioid-active drugs and substances modify the peristaltic reflex by reducing the efficacy of the reflex response and modulating the timing of the reflex pathway. In a second series of expts., luminal application of opioid-active drugs was compared with serosal application. β-Casomorphine-4 caused a concentration-dependent inhibition of the oral reflex response with an IC50 of 3+10-3M which was 750 times higher than after serosal application. In contrast, a stable and highly selective kappa opioid agonist (U-50,488), which caused potent inhibition upon serosal application (IC50: 2.3+10-7M), showed no inhibitory effect after luminal application up to a concentration of 10-2M. Thus casomorphins could have a local effect on the gut wall with no need for systemic absorption. This might be used for a possible therapeutic application.

CC 1-11 (Pharmacology)
ST antidiarrheal oral opioid peristaltic reflex ileum
IT **Intestine**
(ileum; opioid-active therapeutics effect on ascending reflex pathway in ileum)
IT Drug delivery systems
(injections, i.v.; opioid-active therapeutics effect on ascending reflex pathway in ileum)
IT Antidiarrheals
Gastrointestinal motility
(opioid-active therapeutics effect on ascending reflex pathway in ileum)
IT Opioids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(opioid-active therapeutics effect on ascending reflex pathway in ileum)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(opioid-active therapeutics effect on ascending reflex pathway in ileum)

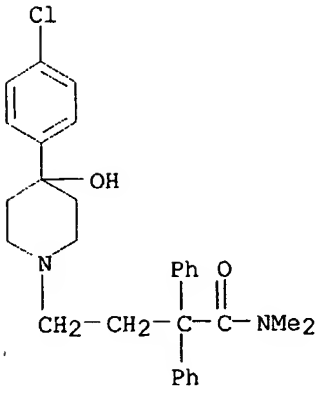
IT Drug delivery systems
(oral; opioid-active therapeutics effect on ascending reflex pathway in ileum)

IT Reflex
(peristaltic; opioid-active therapeutics effect on ascending reflex pathway in ileum)

IT **53179-11-6**, Loperamide **74135-04-9**, β-Casomorphin-4 amide **98815-38-4 123618-00-8**, Fedotozine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid-active therapeutics effect on ascending reflex pathway in ileum)

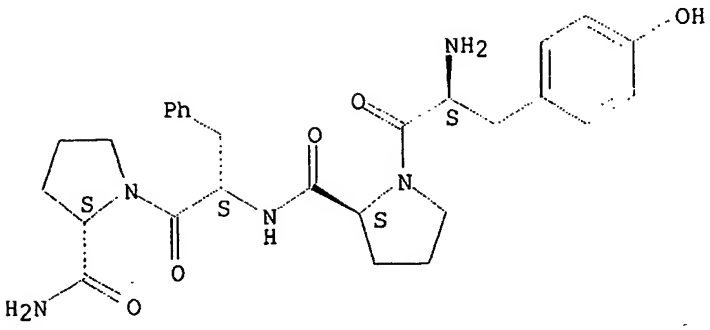
IT **53179-11-6**, Loperamide **74135-04-9**, β-Casomorphin-4 amide **98815-38-4 123618-00-8**, Fedotozine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid-active therapeutics effect on ascending reflex pathway in ileum)

RN 53179-11-6 HCAPLUS
CN 1-Piperidinebutanamide, 4-(4-chlorophenyl)-4-hydroxy-N,N-dimethyl-α,α-diphenyl- (9CI) (CA INDEX NAME)



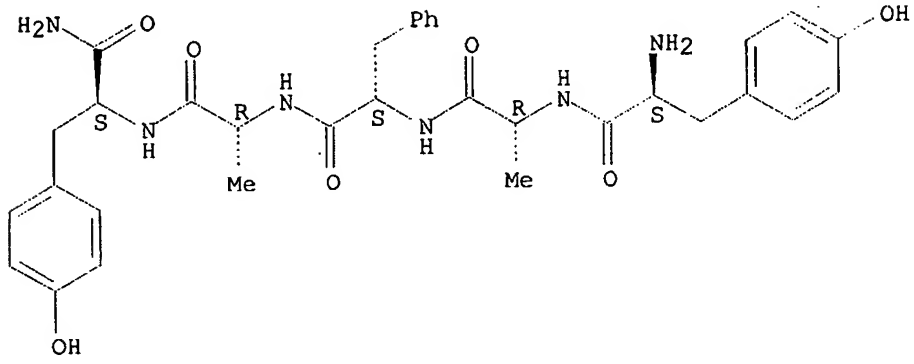
RN 74135-04-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



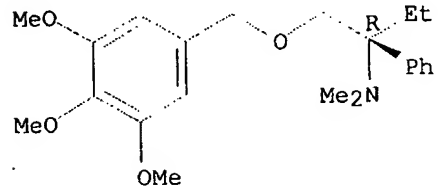
RN 98815-38-4 HCAPLUS
CN L-Tyrosinamide, L-tyrosyl-D-alanyl-L-phenylalanyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 123618-00-8 HCAPLUS
CN Benzenemethanamine, α-ethyl-N,N-dimethyl-α-[[(3,4,5-trimethoxyphenyl)methoxy]methyl]-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



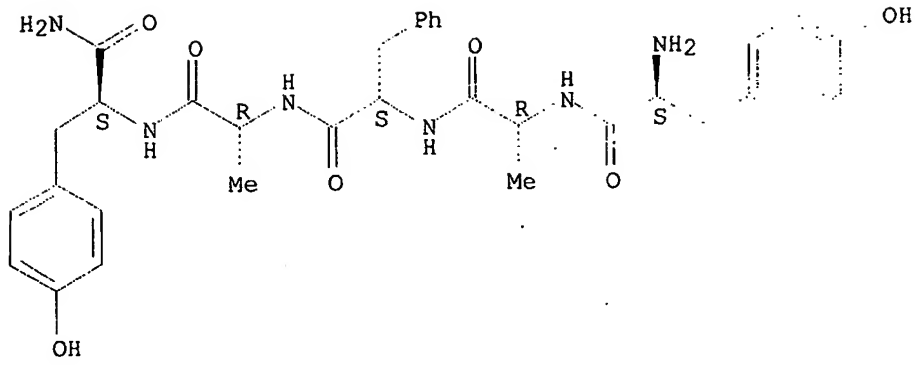
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:285550 HCAPLUS
DOCUMENT NUMBER: 133:84098
TITLE: Effects of oral casokefamide on plasma levels, tolerance, and **intestinal** transit in man
AUTHOR(S): Schulte-Frohlinde, E.; Reindl, W.; Bierling, D.;

Lersch, C.; **Brantl, V.**; Teschemacher, H.; Schusdziarra, V.
CORPORATE SOURCE: Department of Medicine II, Technical University of Munich, Munich, 81675, Germany
SOURCE: Peptides (New York) (2000), 21(3), 439-442
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Food-derived opioid peptides such as β-casomorphins are of interest for treatment of chronic diarrhea. The β-casomorphin analog casokefamide was administered orally at doses of 5.5, 8.0, and 16.0 mg to 10 healthy male volunteers, resp. Dose-dependent increases of plasma levels with a maximum of 350 fmol/l were determined No side-effects due to casokefamide has been observed In comparison to placebo, casokefamide showed a trend toward prolongation of oro-caecal transit time. Orally applied casokefamide is well tolerated and may represent a useful tool for treatment of diarrhea in the future.
CC 1-9 (Pharmacology)
Section cross-reference(s): 2
ST antidiarrheal casokefamide pharmacokinetics tolerance **intestinal** transit
IT Antidiarrheals
Gastrointestinal motility
(effects of oral casokefamide on plasma levels, tolerance, and **intestinal** transit in man)
IT **79805-24-6D**, β-Casomorphin, analogs **98815-38-4**, Casokefamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of oral casokefamide on plasma levels, tolerance, and **intestinal** transit in man)
IT **79805-24-6D**, β-Casomorphin, analogs **98815-38-4**, Casokefamide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of oral casokefamide on plasma levels, tolerance, and **intestinal** transit in man)
RN 79805-24-6 HCAPLUS
CN β-Casomorphin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 98815-38-4 HCAPLUS
CN L-Tyrosinamide, L-tyrosyl-D-alanyl-L-phenylalanyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:351796 HCAPLUS
DOCUMENT NUMBER: 122:157125
TITLE: Effect of bovine β-casomorphin-4-amide on **gastrointestinal** transit and pancreatic endocrine function in man
AUTHOR(S): Schulte-Frohlinde, E.; Schmid, R.; **Brantl, V.** ; Schusdziarra, V.
CORPORATE SOURCE: Department Internal Medicine II, Technical University Munich, Munich, D-8000, Germany
SOURCE: [Beta]-Casomorphins Relat. Pept. [Int. Symp.], 2nd (1994), 155-60
CODEN: 60UMAA
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Opiates are well known therapeutic agents for the treatment of diarrhea and dysentery due to their potent inhibitory effects on **gastrointestinal** motility and secretion. In 8 healthy volunteers the effect of bovine β-casomorphin-4-amide (β-CM-4-NH2) was examined on mouth to cecum transit time by the H2-breath test. All overnight fasted subjects (age 20-29 yr) received either 250, 500 or 750 mg β-CM-4-NH2, or 4 mg loperamide dissolved in 100 mL water 5 min prior to ingestion of 50 g lactulose in 100 mL water. Transit time was delayed by at least 30 % with the 500 and 750 mg β-CM-4-NH2 while 250 mg CM-4-NH2 and 4 mg loperamide had no effect compared to control expts. There was no effect of β-CM-4-NH2 on postprandial pancreatic endocrine function and carbohydrate metabolism These data indicates that β-casomorphins might be of therapeutic usefulness in patients where prolongation of **gastrointestinal** transit is required, e.g. in patients suffering from diarrhea or short bowel syndrome.

CC 13-6 (Mammalian Biochemistry)

ST casomorphin **gastrointestinal** transit pancreas endocrine function; antidiarrhea casomorphin; pancreatic hormone secretion casomorphin

IT Diarrhea
(inhibitors; β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)

IT Blood sugar
Digestive tract
(β-casomorphin-4-amide effect on **gastrointestinal**

transit and pancreatic endocrine function in man in relation to diarrhea treatment)

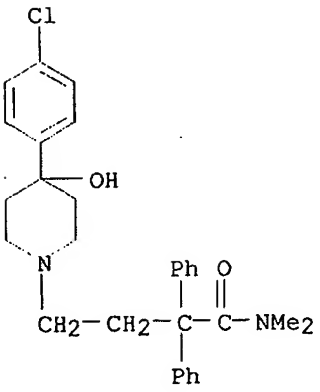
IT Pancreatic hormones
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)

IT **53179-11-6**, Loperamide **74135-04-9**, β-Casomorphin-4-amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)

IT **9004-10-8**, Insulin, biological studies **9007-92-5**, Glucagon, biological studies **59763-91-6**, Pancreatic polypeptide
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)

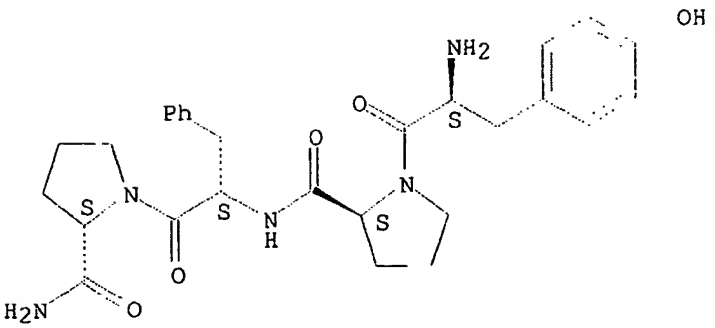
IT **53179-11-6**, Loperamide **74135-04-9**, β-Casomorphin-4-amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)

RN 53179-11-6 HCAPLUS
CN 1-Piperidinebutanamide, 4-(4-chlorophenyl)-4-hydroxy-N,N-dimethyl-α,α-diphenyl- (9CI) (CA INDEX NAME)



RN 74135-04-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9004-10-8**, Insulin, biological studies **9007-92-5**, Glucagon, biological studies **59763-91-6**, Pancreatic polypeptide
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(β-casomorphin-4-amide effect on **gastrointestinal** transit and pancreatic endocrine function in man in relation to diarrhea treatment)
RN 9004-10-8 HCAPLUS
CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9007-92-5 HCAPLUS
CN Glucagon (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 59763-91-6 HCAPLUS
CN Pancreatic polypeptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L28 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:351795 HCAPLUS
DOCUMENT NUMBER: 122:157124
TITLE: Effect of bovine β-casomorphin-4-amide on enteric nerve pathways of the rat ileum
AUTHOR(S): Allescher, H. D.; Piller, C.; **Brantl, V.**; Schusdziarra, V.
CORPORATE SOURCE: Department Internal Medicine II, Technical University Munich, Munich, D-8000/80, Germany
SOURCE: [Beta]-Casomorphins Relat. Pept. [Int. Symp.], 2nd (1994), 150-4
CODEN: 60UMAA
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The ascending excitatory reflex is part of the myenteric reflex, which is a major determinant of **intestinal** propulsion. The aim of the study was to characterize the effect of casomorphin and its analog casomorphin-4-amide on the ascending neural pathways in isolated segments of rat ileum. The gut segments were incubated in an organ bath, stimulated on the anal end by elec. field stimulation of the gut wall (20 V, 3pps. 2 ms) using platinum plates. The excitatory contractile response was recorded manometrically 2 and 4 cm orally to the stimulation site. The induced contractile response was inhibited via a naloxone-sensitive mechanism by serosal application of casomorphin and casomorphin-4-amide. However, the inhibition was less potent when compared to serosal

application of the selective kappa opioid agonist U-50,488. On the contrary, when the substances were applied intraluminally casomorphin and casomorphin-4-amide still decreased the induced contractile activity, but with this mode of application were more potent than the selective kappa opioid agonist U-50,488, which was almost inactive when applied intraluminally. These results demonstrate that casomorphins can inhibit **intestinal** motility from the serosal and the luminal side. The inhibitory effect when applied luminally could be due to a specific mode of action of casomorphins on the mucosa or mucosal nerve endings.

CC 13-6 (Mammalian Biochemistry)

ST beta casomorphin enteric nerve ileum

IT Opioids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endogenous, β-casomorphin-4-amide effect on enteric nerve pathways of ileum mediation by opioids)

IT Nerve
(enteric, β-casomorphin-4-amide effect on enteric nerve pathways of ileum)

IT **Intestine**
(ileum, β-casomorphin-4-amide effect on enteric nerve pathways of ileum)

IT Reflex
(peristaltic, β-casomorphin-4-amide effect on enteric nerve pathways of ileum)

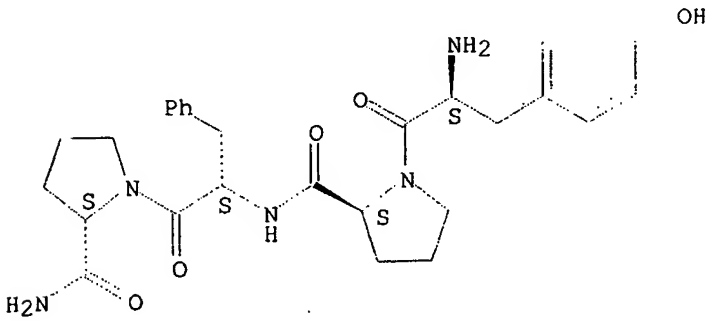
IT **74135-04-9**, β-Casomorphin-4-amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(β-casomorphin-4-amide effect on enteric nerve pathways of ileum)

IT **74135-04-9**, β-Casomorphin-4-amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(β-casomorphin-4-amide effect on enteric nerve pathways of ileum)

RN 74135-04-9 HCAPLUS

CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:351794 HCAPLUS

DOCUMENT NUMBER: 122:151663

TITLE: β-Casomorphins and **intestinal** net fluid transport in vivo

AUTHOR(S): Erll, G.; Hahn, A.; **Brantl, V.**; Daniel, H.

CORPORATE SOURCE: Institute Nutrition, Justus-Liebig-University,

Giessen, D-6300, Germany
SOURCE: [Beta]-Casomorphins Relat. Pept. [Int. Symp.], 2nd (1994), 143-9
CODEN: 60UMAA
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The antisecretory activities of morphiceptin (bovine β-casomorphin-4-amide) and the synthetic β-casomorphin analog casokefamide (D-Ala2,4,Tyr5-β-casomorphin-5-amide) were examined in vivo in ligated loops prepared from the proximal jejunum of rats. Net fluid secretion was induced by a heat-stable E.coli toxin in combination with theophylline. Luminal administration of morphiceptin revealed a significant antisecretory effect at relatively low concns. (10-7 and 10-6M). In contrast, higher concns. (10-5 - 10-2M) failed to alter fluid movement. Morphiceptin at a concentration of 10-6 M was equally effective as a single dose of loperamide (4 mg/kg b.w.). When casokefamide was given into the **intestinal** lumen there was a significant reduction of fluid secretion at 10-3 M but not at higher or lower concns., resp. Because coadministration of naloxone with the β-casomorphins caused a significant increase in fluid secretion rate as compared with controls the authors suggest that, besides opioid-specific antisecretory effects, β-casomorphins can addnl. elicit non-opioid secretory effects.

CC 2-5 (Mammalian Hormones)

ST beta casomorphin **intestine** fluid transport opioid; antidiarrhea morphiceptin casokefamide

IT Diarrhea
(antidiarrheals; casokefamide and morphiceptin antidiarrheal activity)

IT Escherichia coli
(β-casomorphins effects on **intestinal** fluid transport induced by endotoxins)

IT **Intestine**
(β-casomorphins effects on **intestinal** fluid transport mediation by opioid and non-opioid mechanisms)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(endo-, β-casomorphins effects on **intestinal** fluid transport induced by endotoxins)

IT Opioids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endogenous, β-casomorphins effects on **intestinal** fluid transport mediation by opioid and non-opioid mechanisms)

IT **Intestine**
(jejunum, proximal, β-casomorphins effects on **intestinal** fluid transport mediation by opioid and non-opioid mechanisms)

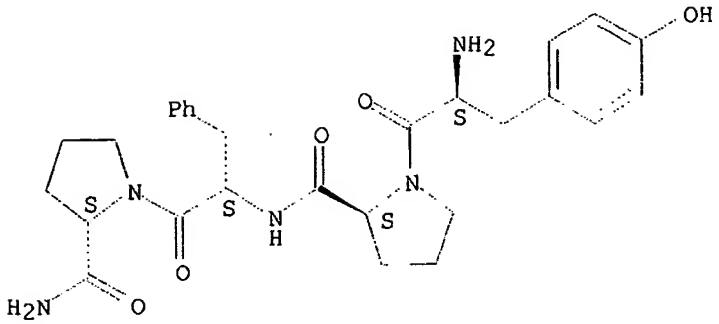
IT **74135-04-9**, Morphiceptin **98815-38-4**, Casokefamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(casokefamide and morphiceptin antidiarrheal activity)

IT **74135-04-9**, Morphiceptin **98815-38-4**, Casokefamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(casokefamide and morphiceptin antidiarrheal activity)

RN 74135-04-9 HCAPLUS

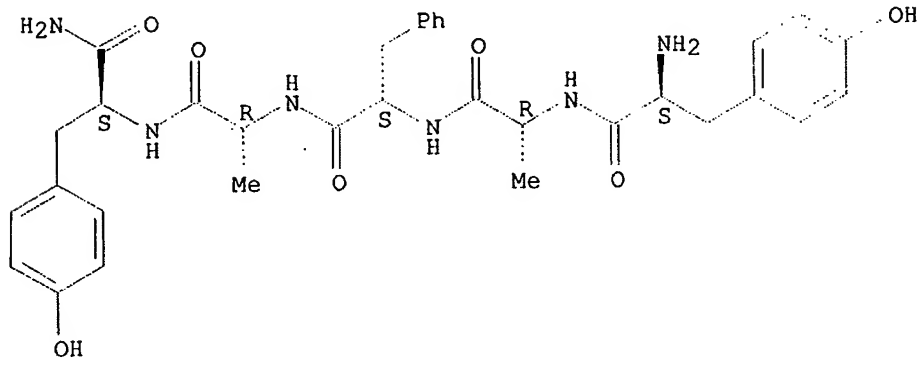
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 98815-38-4 HCAPLUS
CN L-Tyrosinamide, L-tyrosyl-D-alanyl-L-phenylalanyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:805 HCAPLUS
DOCUMENT NUMBER: 114:805
TITLE: Absorption of β-casomorphins from autoperfused lamb and piglet small **intestine**
AUTHOR(S): Read, Leanna C.; Lord, Andrew P. D.; **Brantl, Victor**; Koch, Gertrud
CORPORATE SOURCE: Waite Agric. Res. Inst., Univ. Adelaide, Glen Osmond, 5064, Australia
SOURCE: American Journal of Physiology (1990), 259(3, Pt. 1), G443-G452
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB β-Casomorphins (β-CMs) derived from milk β-casein may exert various opiate activities in milk-fed infants. To assess the physiol. significance of β-CMs as a source of circulating opioids in infants, absorption rates of several β-CMs were determined under near-physiol. conditions using in situ autoperfused lamb **intestine**. The naturally occurring β-CMs, β-CM-7 and β-CM-4-amide, were absorbed readily into blood with no transfer into lymph. Uptake peaked within several minutes of the luminal infusion of peptide but then declined sharply and stopped within a further 10-15 min. The recovery in

blood, **intestinal** contents, and tissue at the end of the 30-min experiment was <1% of the infused dose. The low recovery was due to rapid proteolysis based on in vitro studies that demonstrated half-lives of <5 min in lamb blood, luminal contents, and lymph. The synthetic dipeptidyl peptidase IV-resistant analog β-[D-Ala2]CM-4-amide was stable during incubation in blood, lymph, or luminal contents and was absorbed into blood at rates that were maximal within several minutes and remained steady for the 30 min. Although natural β-CMs are transferred across the lamb small **intestine**, rapid degradation within the **intestinal** lumen, gut epithelium, and blood would prevent entry into the circulation under normal conditions. Val-β-CM-7, a putative stable precursor, had similar stability and kinetics of absorption to β-CM-7, results that exclude Val-β-CM-7 as a stable precursor for delivery of β-CMs to the circulation. Essentially identical results to those in lambs were obtained in 7-day-old piglets.

CC 2-5 (Mammalian Hormones)

ST casomorphin **intestine** absorption newborn

IT Newborn
(β-casomorphins absorption by small **intestine** of)

IT **Intestine**, metabolism
(small, β-casomorphins absorption by, of newborn)

IT **72122-62-4 74135-04-9 79805-24-6D**,
β-Casomorphin, derivs. **83936-20-3 130968-81-9**
RL: PROC (Process)
(absorption of, by small **intestine** of newborn)

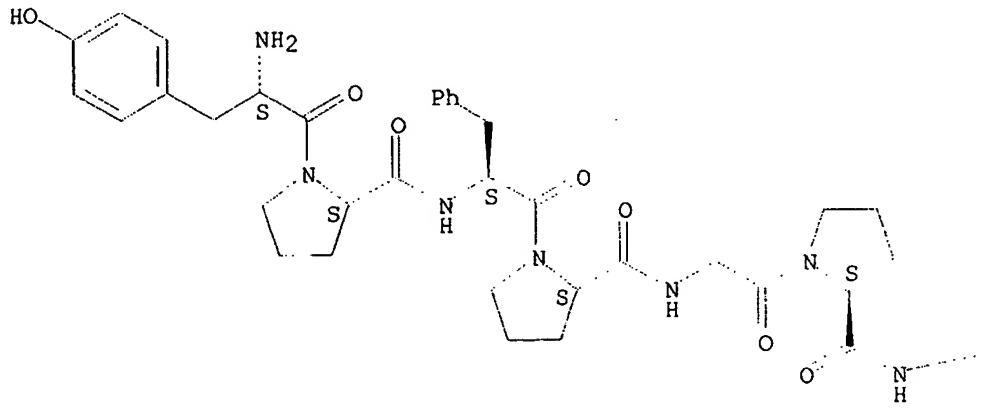
IT **72122-62-4 74135-04-9 79805-24-6D**,
β-Casomorphin, derivs. **83936-20-3 130968-81-9**
RL: PROC (Process)
(absorption of, by small **intestine** of newborn)

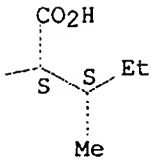
RN 72122-62-4 HCAPLUS

CN L-Isoleucine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

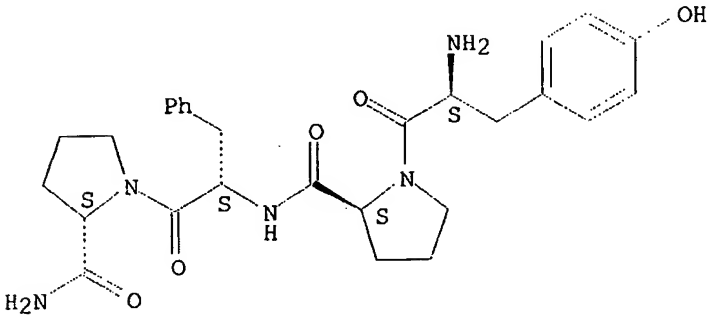
PAGE 1-A





RN 74135-04-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

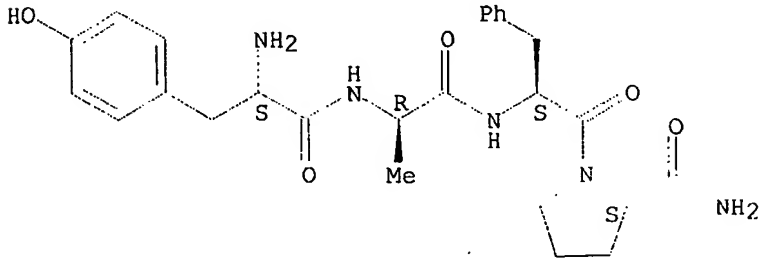
Absolute stereochemistry.



RN 79805-24-6 HCAPLUS
CN β-Casomorphin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 83936-20-3 HCAPLUS
CN L-Prolinamide, L-tyrosyl-D-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

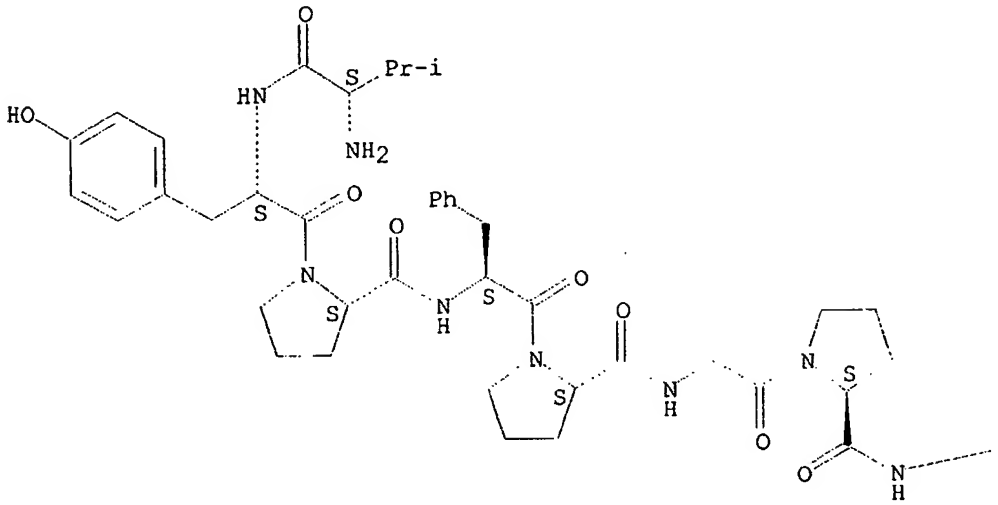
Absolute stereochemistry.



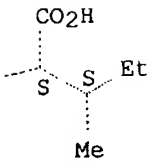
RN 130968-81-9 HCAPLUS
CN L-Isoleucine, L-valyl-L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L28 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:187282 HCAPLUS

DOCUMENT NUMBER: 108:187282
TITLE: Preparation of L-tyrosyl-L-prolyl-L-phenyl-L-alanyl-L-threonine and homologs as drugs
INVENTOR(S): **Brantl, Victor**
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3514587	A1	19861030	DE 1985-3514587	19850423
EP 199331	A1	19861029	EP 1986-105507	19860421
EP 199331	B1	19890906		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
WO 8606381	A1	19861106	WO 1986-DE169	19860421
W: JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 218650	A1	19870422	EP 1986-902336	19860421
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 62501422	T2	19870611	JP 1986-502293	19860421
AT 46173	E	19890915	AT 1986-105507	19860421
PRIORITY APPLN. INFO.:			DE 1985-3514587	19850423
			EP 1986-105507	19860421
			WO 1986-DE169	19860421

AB H-Tyr-Pro-Phe-Thr-A-B-C-D-E-T [I; A, B, C, D, E = D-or L-amino acid residue, bond; T = OH, OR, NH, NHR, NR2, NHNHR2; R = C1-10 alkyl, adamantyl, cycloalkyl, aralkyl, Ph; R2 = H, C1-10 alkyl, cycloalkyl, aralkyl, (substituted) acyl, carbamoyl] were prepared as drugs with central nervous system, endocrine, immunomodulatory, metabolic, and antigenic activities. Thus, H-Tyr-Pro-Phe-Thr-OH (II) was prepd by the solution-phase method using benzyloxycarbonyl-protected amino acids as mixed anhydrides. II had an IC50 of 120.1 μM in a test of inhibition of elec.-induced contraction of guinea pig **intestinal** tissue, vs. 0.1 μM for normorphine.

IC ICM C07C007-06
ICS C07K005-10; A61K037-02; A61K037-18

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST tyrosylprolylphenylalanylthreonine prepn drug; immunomodulator prepn peptide; central nervous system agent prepn peptide

IT Pharmaceuticals
(peptides)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of tyrosylprolylphenylalanylthreonine and homologs as drugs)

IT Analgesics
Immunomodulators
Nervous system agents
(tyrosylprolylphenylalanylthreonine and homologs)

IT **17350-17-3 18598-74-8 29713-96-0**
RL: PROC (Process)
(conversion of, to mixed anhydride)

IT **543-27-1**
RL: PROC (Process)
(conversion of, to mixed anhydride with prolyphenylalanine derivative)

IT **2577-46-0 19728-63-3 39994-75-7**

114102-50-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, in preparation of drug)

IT **114102-53-3P 114102-54-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of, in preparation of drug)

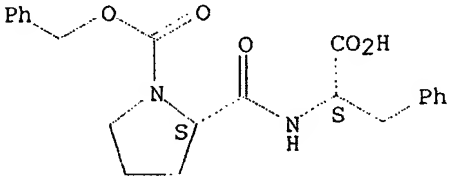
IT **97730-74-0P 97730-75-1P 114102-28-2P**
114102-29-3P 114102-30-6P 114102-31-7P
114102-32-8P 114102-33-9P 114102-34-0P
114102-35-1P 114102-36-2P 114102-37-3P
114102-38-4P 114102-39-5P 114102-40-8P
114102-41-9P 114102-42-0P 114102-43-1P
114102-44-2P 114102-45-3P 114135-32-9P
114180-91-5P 114180-92-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

IT **114102-46-4P 114102-47-5P 114102-48-6P**
114102-49-7P 114102-51-1P 114102-52-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as drug intermediate)

IT **17350-17-3 18598-74-8 29713-96-0**
RL: PROC (Process)
(conversion of, to mixed anhydride)

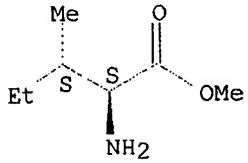
RN 17350-17-3 HCAPLUS
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 18598-74-8 HCAPLUS
CN L-Isoleucine, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

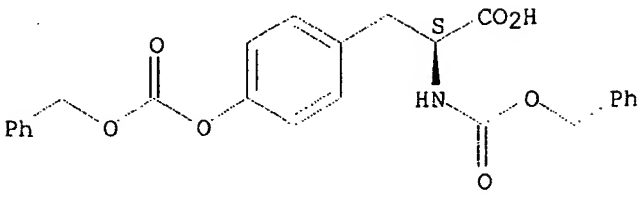
Absolute stereochemistry. Rotation (+).



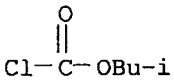
● HCl

RN 29713-96-0 HCAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, phenylmethyl carbonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

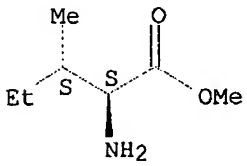


IT **543-27-1**
RL: PROC (Process)
(conversion of, to mixed anhydride with prolyphenylalanine derivative)
RN 543-27-1 HCAPLUS
CN Carbonochloridic acid, 2-methylpropyl ester (9CI) (CA INDEX NAME)



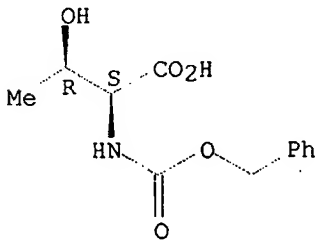
IT **2577-46-0 19728-63-3 39994-75-7**
114102-50-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, in preparation of drug)
RN 2577-46-0 HCAPLUS
CN L-Isoleucine, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



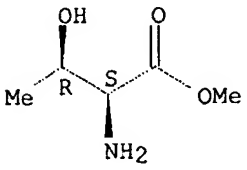
RN 19728-63-3 HCAPLUS
CN L-Threonine, N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 39994-75-7 HCAPLUS
CN L-Threonine, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

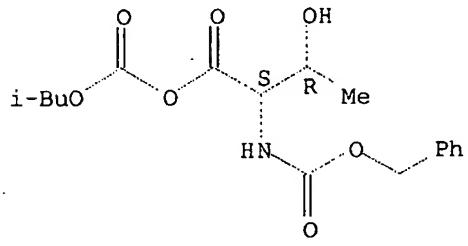
Absolute stereochemistry.



● HCl

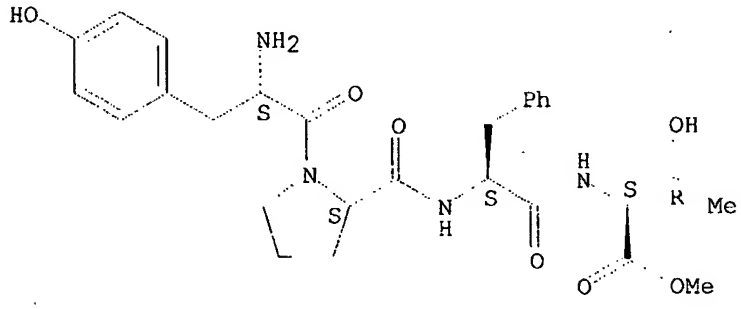
RN 114102-50-0 HCAPLUS
CN L-Threonine, N-[(phenylmethoxy)carbonyl]-, anhydride with 2-methylpropyl hydrogen carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



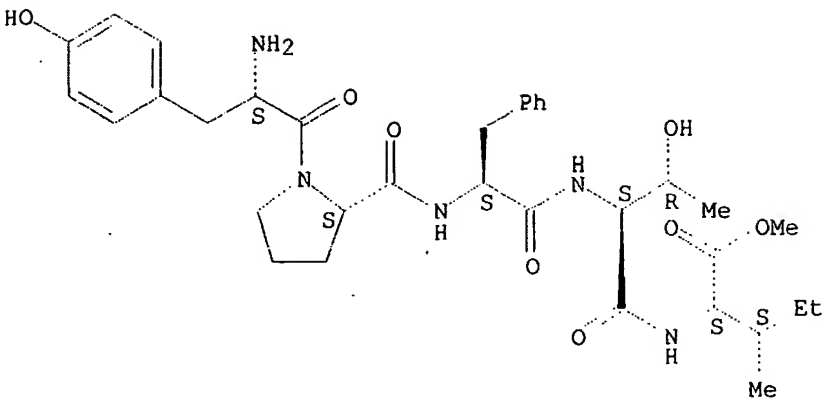
IT **114102-53-3P 114102-54-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of, in preparation of drug)
RN 114102-53-3 HCAPLUS
CN L-Threonine, N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



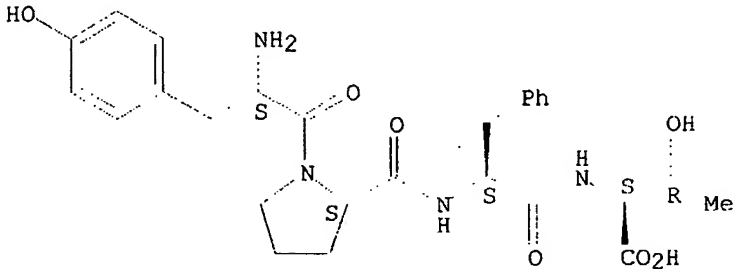
RN 114102-54-4 HCAPLUS
CN L-Isoleucine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



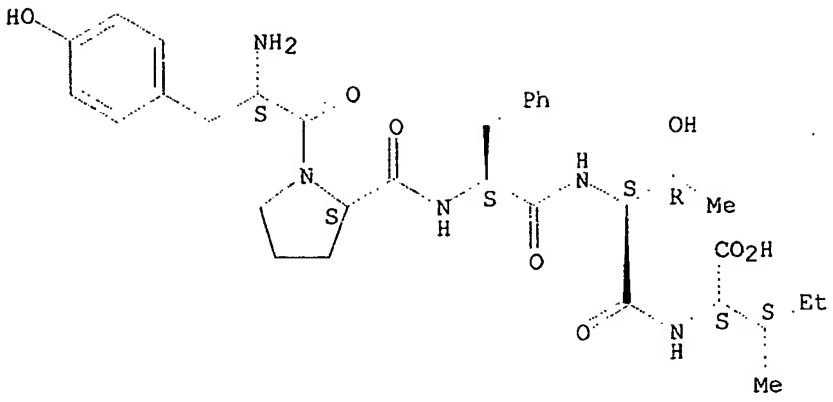
IT **97730-74-0P 97730-75-1P 114102-28-2P**
114102-29-3P 114102-30-6P 114102-31-7P
114102-32-8P 114102-33-9P 114102-34-0P
114102-35-1P 114102-36-2P 114102-37-3P
114102-38-4P 114102-39-5P 114102-40-8P
114102-41-9P 114102-42-0P 114102-43-1P
114102-44-2P 114102-45-3P 114135-32-9P
114180-91-5P 114180-92-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
RN 97730-74-0 HCAPLUS
CN L-Threonine, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



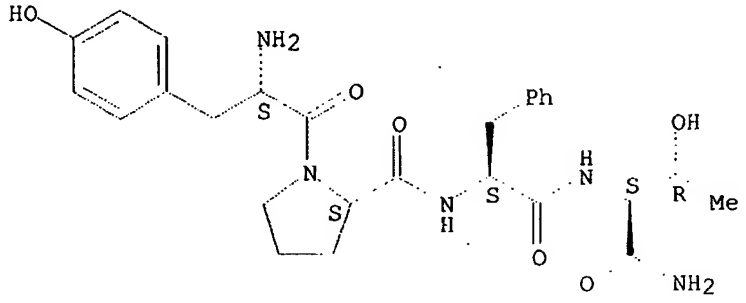
RN 97730-75-1 HCAPLUS
CN L-Isoleucine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



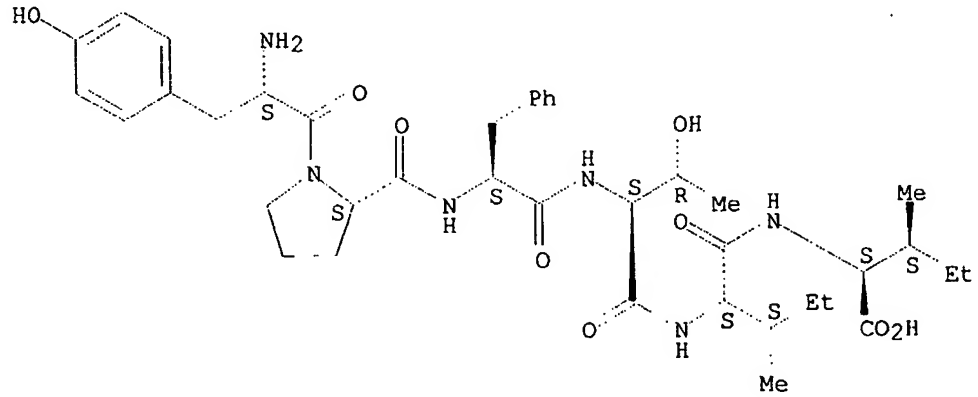
RN 114102-28-2 HCAPLUS
CN L-Threoninamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 114102-29-3 HCAPLUS
CN L-Isoleucine, N-[N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-L-isoleucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

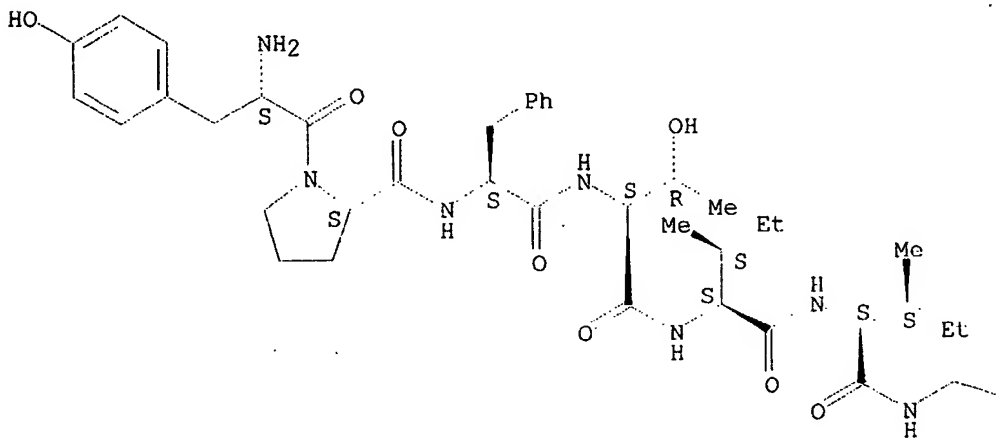


RN 114102-30-6 HCAPLUS

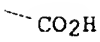
CN Glycine, N-[N-[N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-L-isoleucyl]-L-isoleucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



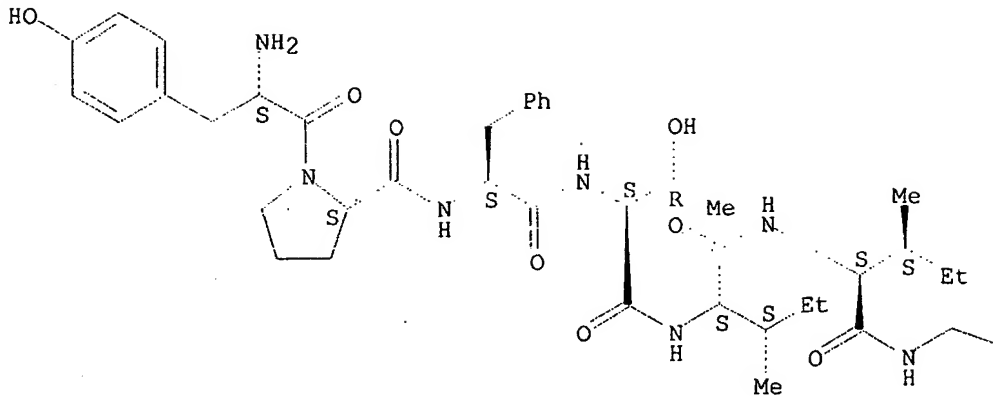
PAGE 1-B



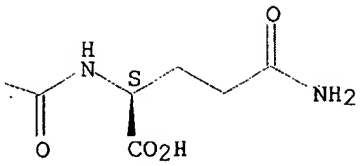
RN 114102-31-7 HCAPLUS
CN L-Glutamine, N2-[N-[N-[N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-L-isoleucyl]-L-isoleucyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



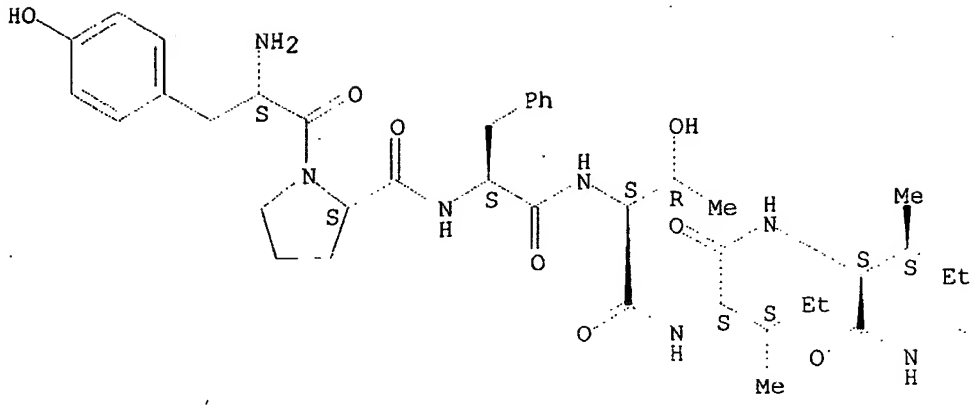
PAGE 1-B



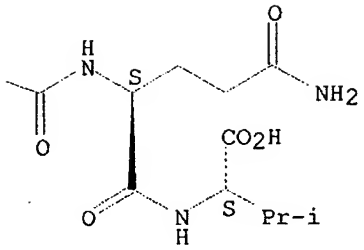
RN 114102-32-8 HCAPLUS
CN L-Valine, N-[N2-[N-[N-[N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-L-isoleucyl]-L-isoleucyl]glycyl]-L-glutaminyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

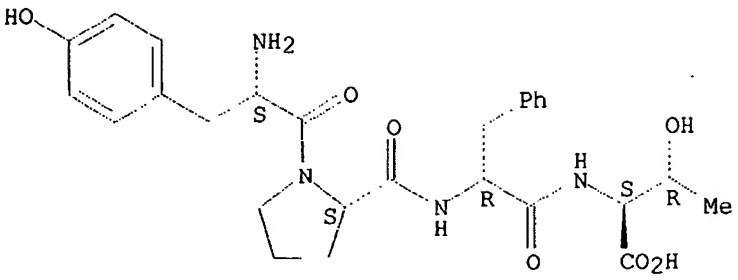


PAGE 1-B



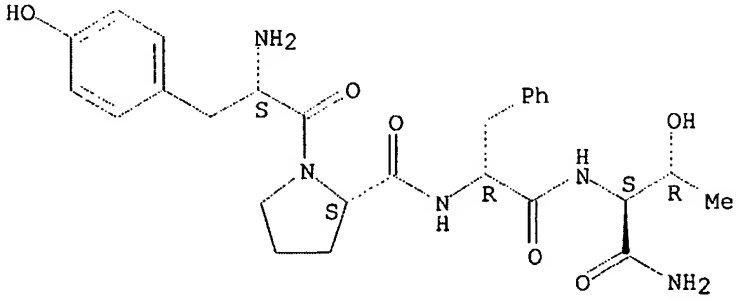
RN 114102-33-9 HCAPLUS
CN L-Threonine, N-[N-(1-L-tyrosyl-L-prolyl)-D-phenylalanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



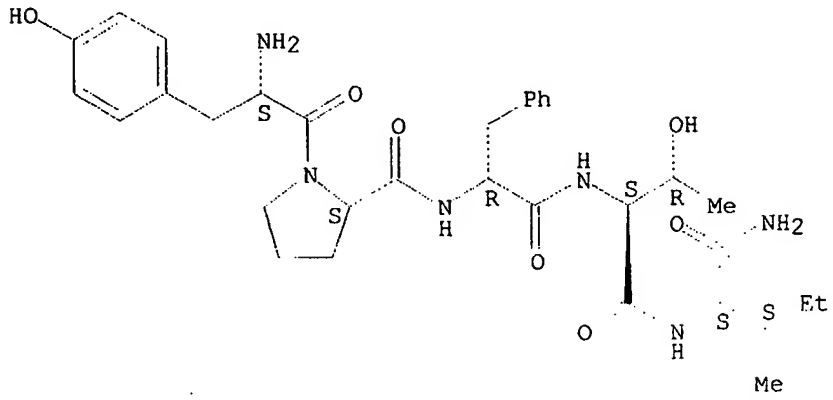
RN 114102-34-0 HCAPLUS
CN L-Threoninamide, L-tyrosyl-L-prolyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



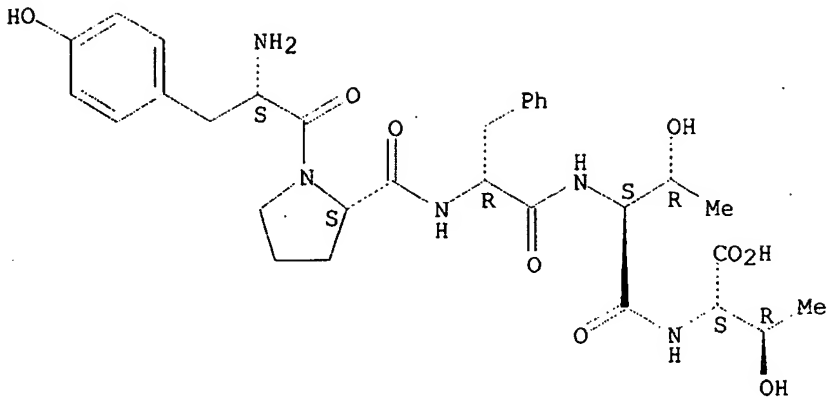
RN 114102-35-1 HCAPLUS
CN L-Isoleucinamide, L-tyrosyl-L-prolyl-D-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



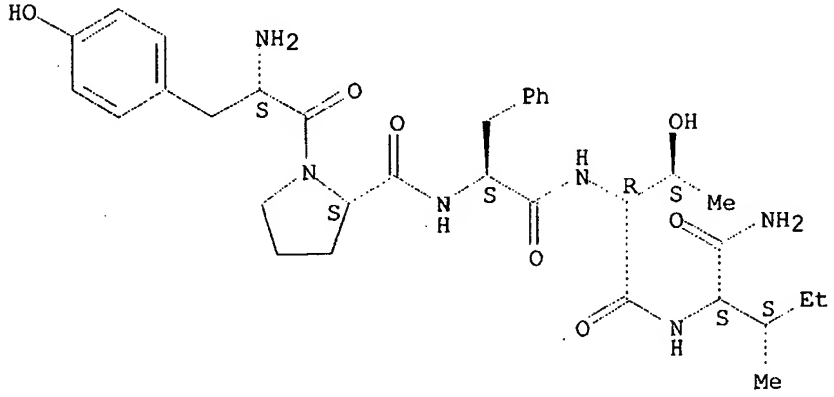
RN 114102-36-2 HCAPLUS
CN L-Threonine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-D-phenylalanyl]-L-threonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



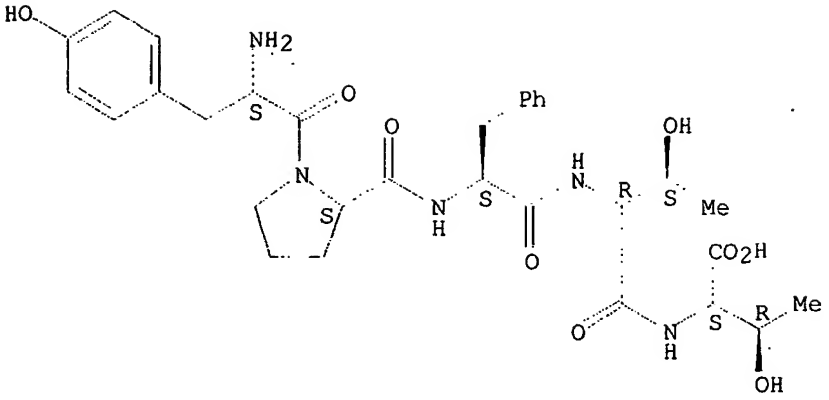
RN 114102-37-3 HCAPLUS
CN L-Isoleucinamide, L-tyrosyl-L-prolyl-L-phenylalanyl-D-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



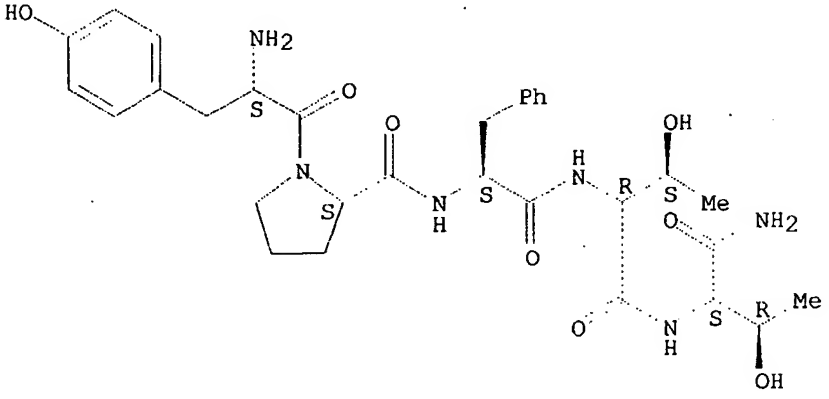
RN 114102-38-4 HCAPLUS
CN L-Threonine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-D-threonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



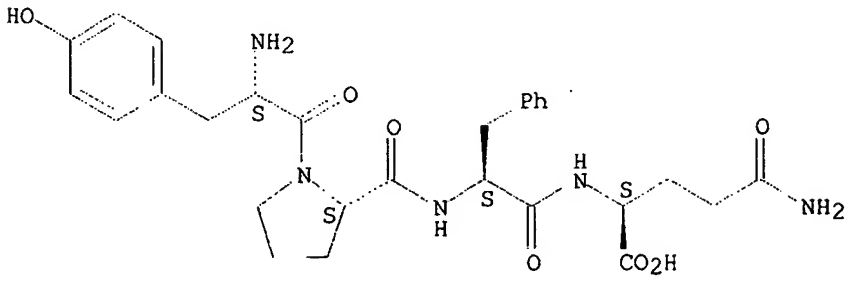
RN 114102-39-5 HCAPLUS
CN L-Threoninamide, L-tyrosyl-L-prolyl-L-phenylalanyl-D-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 114102-40-8 HCAPLUS
CN L-Glutamine, N2-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]- (9CI) (CA INDEX NAME)

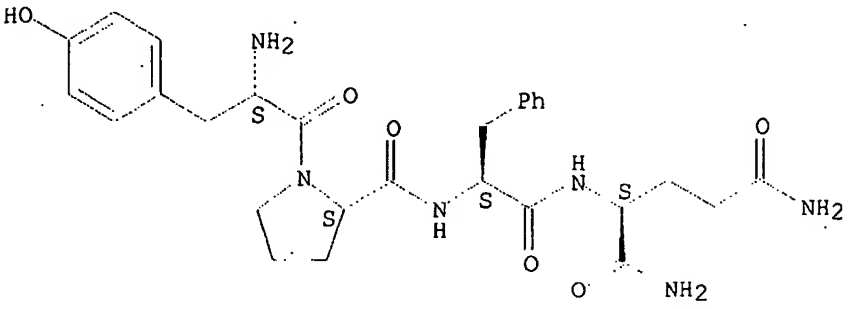
Absolute stereochemistry.



RN 114102-41-9 HCAPLUS

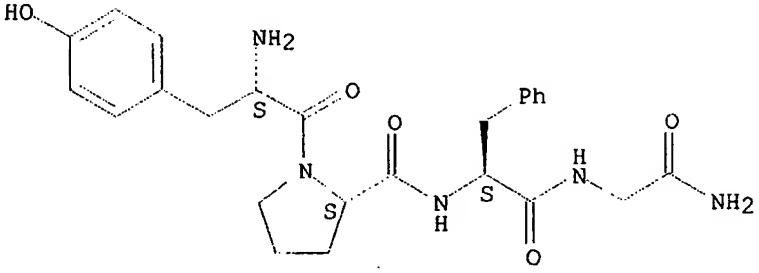
CN L-Glutamamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



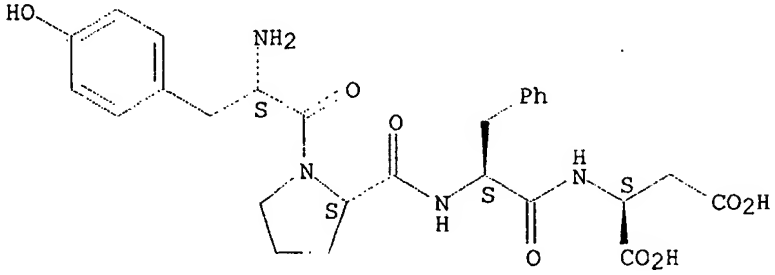
RN 114102-42-0 HCAPLUS
CN Glycinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



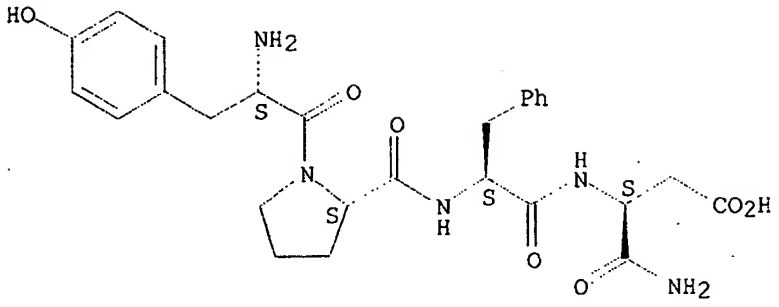
RN 114102-43-1 HCAPLUS
CN L-Aspartic acid, N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



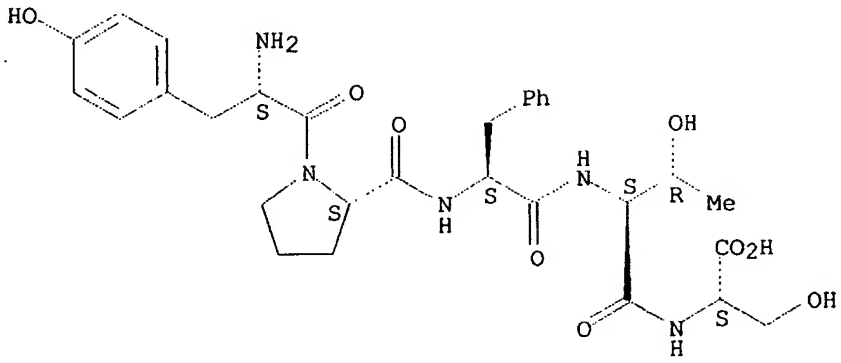
RN 114102-44-2 HCAPLUS
CN L-α-Asparagine, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



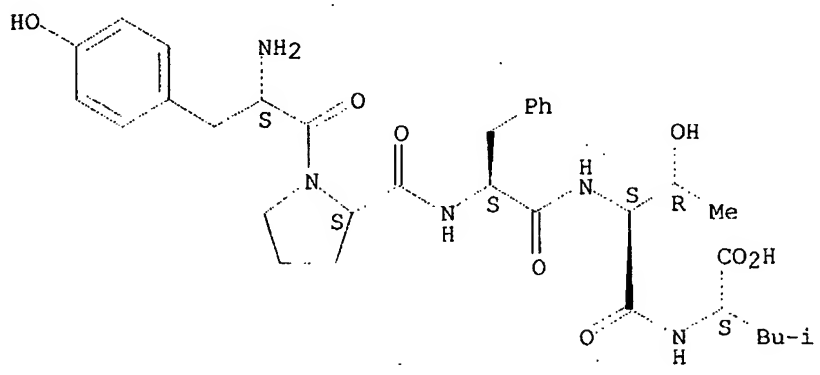
RN 114102-45-3 HCAPLUS
CN L-Serine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 114135-32-9 HCAPLUS
CN L-Leucine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-
(9CI) (CA INDEX NAME)

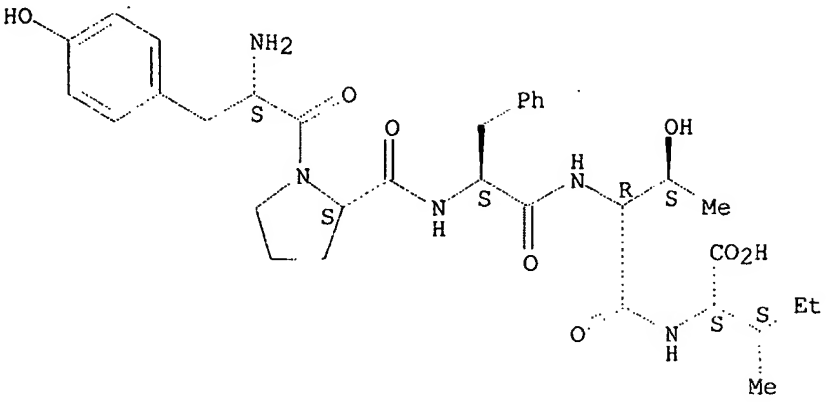
Absolute stereochemistry.



RN 114180-91-5 HCAPLUS
CN L-Isoleucine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-D-threonyl]-

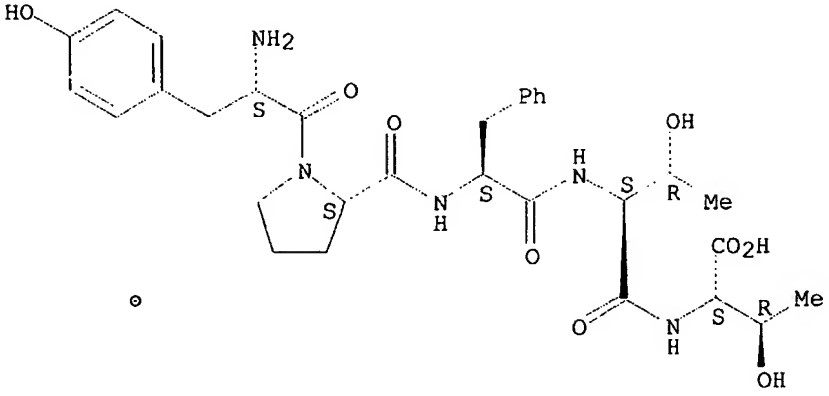
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



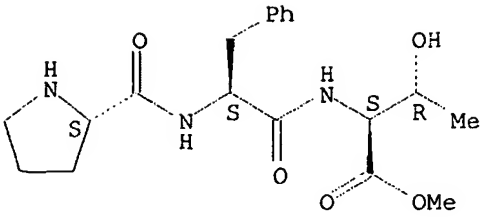
RN 114180-92-6 HCAPLUS
CN L-Threonine, N-[N-[N-(1-L-tyrosyl-L-prolyl)-L-phenylalanyl]-L-threonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



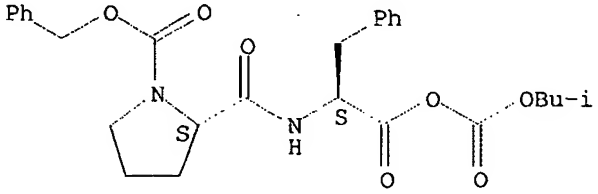
IT **114102-46-4P 114102-47-5P 114102-48-6P**
114102-49-7P 114102-51-1P 114102-52-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as drug intermediate)
RN 114102-46-4 HCAPLUS
CN L-Threonine, N-(N-L-prolyl-L-phenylalanyl)-, methyl ester (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



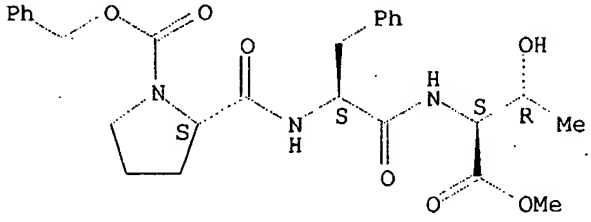
RN 114102-47-5 HCAPLUS
CN L-Phenylalanine, N-[1-[(phenylmethoxy)carbonyl]-L-prolyl]-, anhydride with 2-methylpropyl hydrogen carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



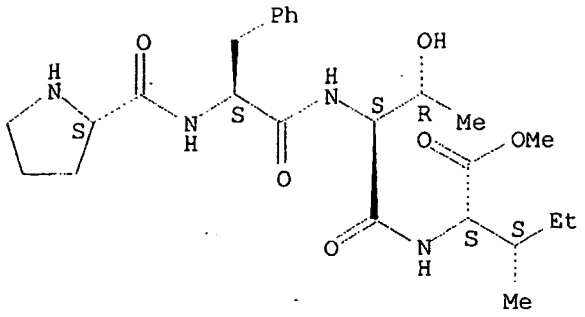
RN 114102-48-6 HCAPLUS
CN L-Threonine, N-[N-[1-[(phenylmethoxy)carbonyl]-L-prolyl]-L-phenylalanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



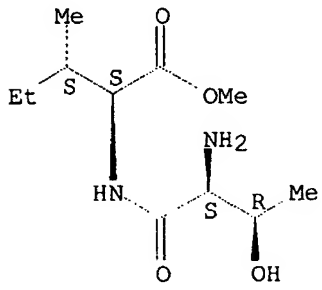
RN 114102-49-7 HCAPLUS
CN L-Isoleucine, N-[N-(N-L-prolyl-L-phenylalanyl)-L-threonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



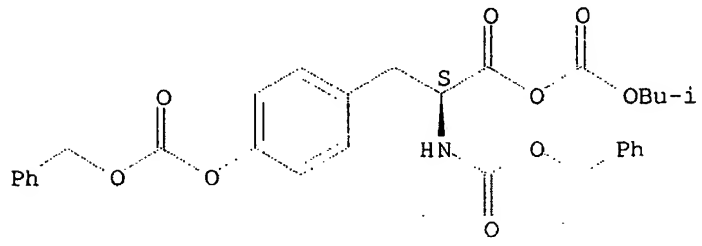
RN 114102-51-1 HCAPLUS
CN L-Isoleucine, N-L-threonyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 114102-52-2 HCAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, anhydride with 2-methylpropyl hydrogen carbonate, phenylmethyl carbonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:75861 HCAPLUS
DOCUMENT NUMBER: 108:75861
TITLE: Preparation of tyrosylprolyltryptophanylthreonyl-containing peptides as drugs
INVENTOR(S): **Brantl, Victor**
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

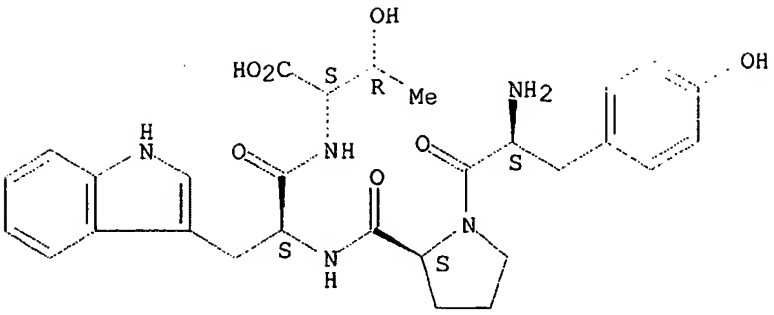
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3618407	A1	19871203	DE 1986-3618407	19860531
EP 248231	A2	19871209	EP 1987-106649	19870507
EP 248231	A3	19900509		
EP 248231	B1	19930728		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 92078	E	19930815	AT 1987-106649	19870507
JP 62286997	A2	19871212	JP 1987-112229	19870508

PRIORITY APPLN. INFO.: DE 1986-3618407 19860531
EP 1987-106649 19870507

AB H-Tyr-Pro-Trp-Thr-X-T (I; T = OH, OR, NH2, NHR, NR2, NHNHR2; R = substituted alkyl, adamantyl, cycloalkyl, Ph, aralkyl; R2 = H, alkyl, cycloalkyl, aralkyl, acyl, alkylcarbamoyl; X = 0-6 D-ro L-amino acid residues) and their pharmaceutically acceptable salts were prepared as drugs. H-Tyr-Pro-Trp-Thr-OH (II) was prepared by the solid phase method using FMOC-protected amino acids. II inhibited elec.-induced contractions of guinea pig **intestine** with an IC50 of 45.2 μM, vs. 0.1 μM for normorphine.

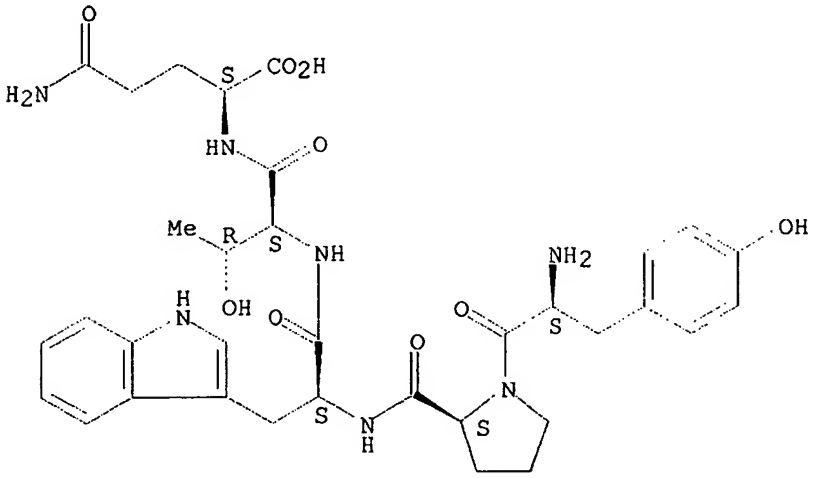
IC ICM C07K007-06
ICS A61K037-02; G01N033-68
ICA C07K015-06
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptide prepn drug; tyrosylprolyltryptophanylthreonyl contg peptide prepn drug; analgesic tyrosylprolyltryptophanylthreonyl contg peptide; tranquilizer tyrosylprolyltryptophanylthreonyl contg peptide
IT Analgesics
(tyrosylprolyltryptophanylthreonine containing peptides)
IT **103930-64-9P 103930-65-0P 112747-34-9P**
112747-35-0P 112747-36-1P 112747-37-2P
112747-38-3P 112747-39-4P 112747-40-7P
112747-41-8P 112747-42-9P 112747-43-0P
112747-44-1P 112747-45-2P 112765-57-8P
112765-58-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
IT **103930-64-9P 103930-65-0P 112747-34-9P**
112747-35-0P 112747-36-1P 112747-37-2P
112747-38-3P 112747-39-4P 112747-40-7P
112747-41-8P 112747-42-9P 112747-43-0P
112747-44-1P 112747-45-2P 112765-57-8P
112765-58-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
RN 103930-64-9 HCAPLUS
CN L-Threonine, L-tyrosyl-L-prolyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



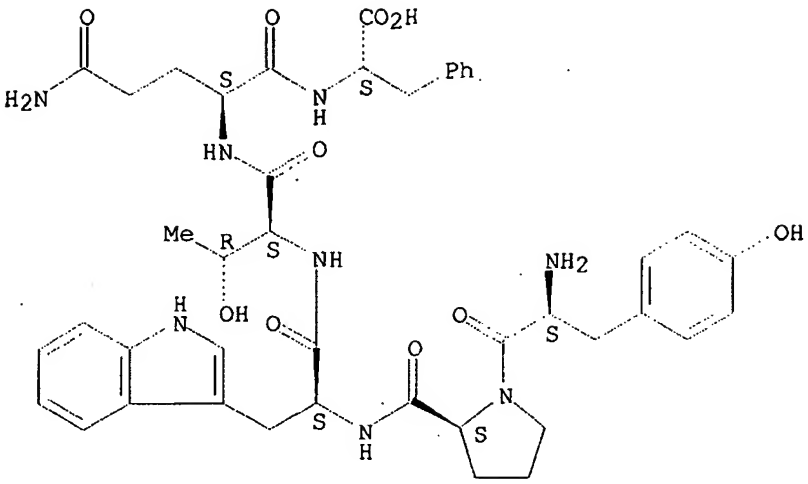
RN 103930-65-0 HCAPLUS
CN L-Glutamine, L-tyrosyl-L-prolyl-L-tryptophyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



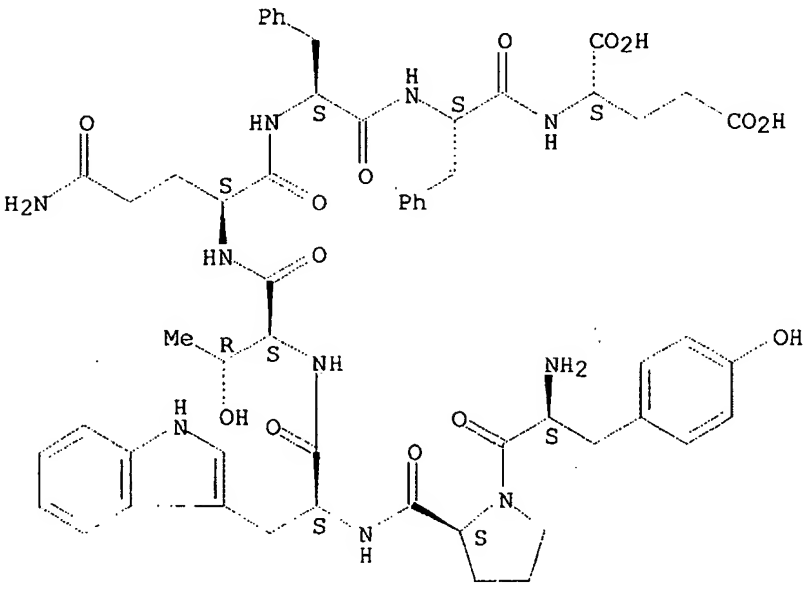
RN 112747-34-9 HCAPLUS
CN L-Phenylalanine, N-[N2-[N-[N-(1-L-tyrosyl-L-prolyl)-L-tryptophyl]-L-threonyl]-L-glutaminyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 112747-35-0 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N2-[N-[N-(1-L-tyrosyl-L-prolyl)-L-tryptophyl]-L-threonyl]-L-glutaminyl]-L-phenylalanyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)

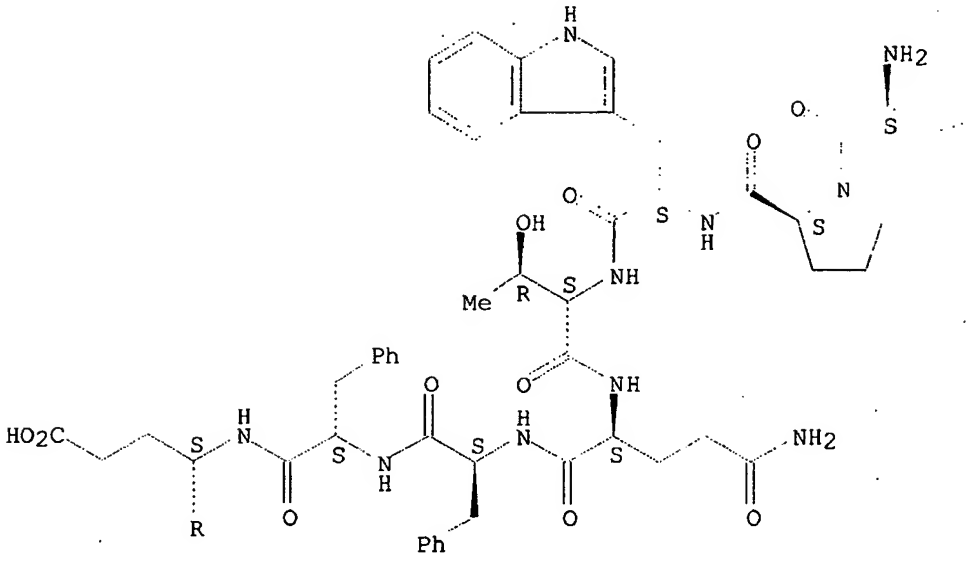
Absolute stereochemistry.



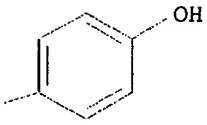
RN 112747-36-1 HCAPLUS
CN L-Aspartic acid, N-[N-[N-[N-[N2-[N-[N-(1-L-tyrosyl-L-prolyl)-L-tryptophyl]-L-threonyl]-L-glutaminyl]-L-phenylalanyl]-L-phenylalanyl]-L-α-glutamyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

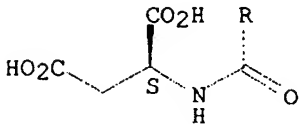
PAGE 1-A



PAGE 1-B



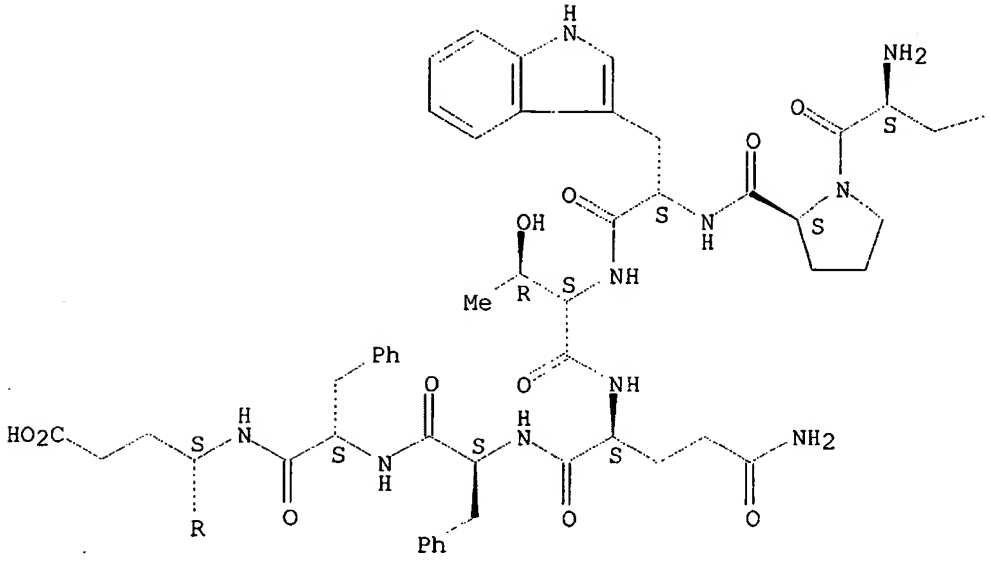
PAGE 2-A



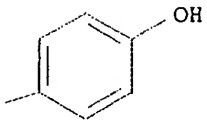
RN 112747-37-2 HCAPLUS
CN L-Serine, N-[N-[N-[N-[N2-[N-[N-(1-L-tyrosyl-L-prolyl)-L-tryptophyl]-L-threonyl]-L-glutaminyl]-L-phenylalanyl]-L-phenylalanyl]-L-α-glutamyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

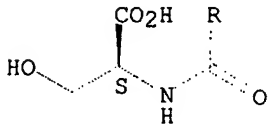
PAGE 1-A



PAGE 1-B

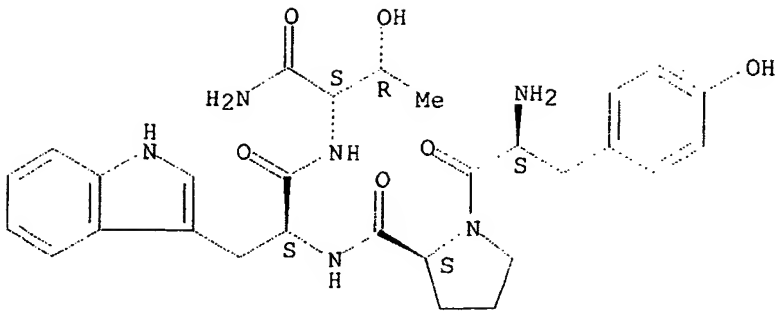


PAGE 2-A



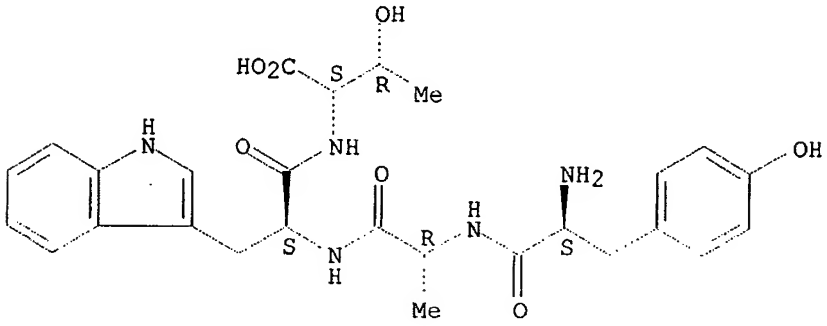
RN 112747-38-3 HCAPLUS
CN L-Threoninamide, L-tyrosyl-L-prolyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



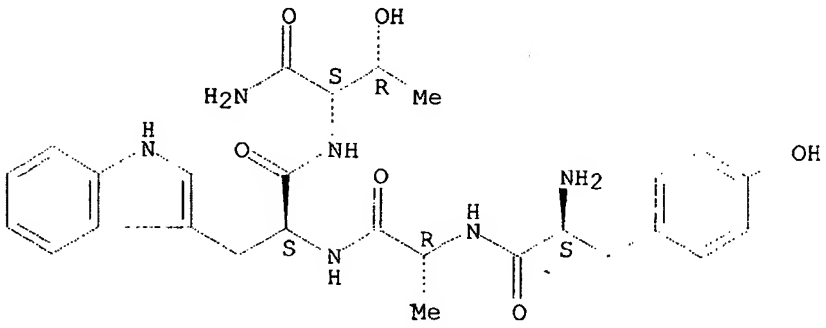
RN 112747-39-4 HCAPLUS
CN L-Threonine, N-[N-(N-L-tyrosyl-D-alanyl)-L-tryptophyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



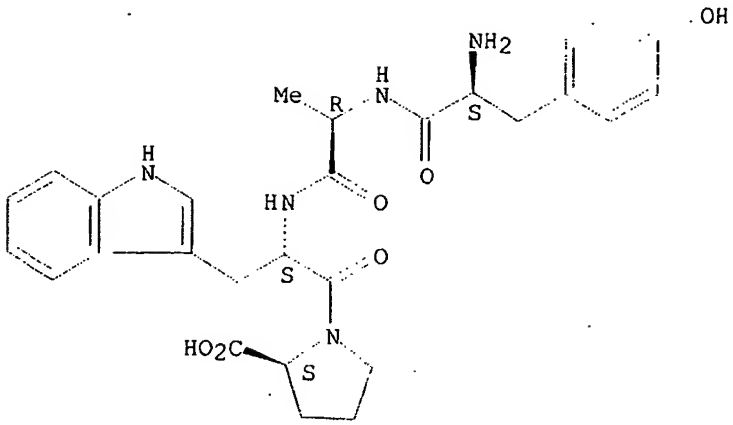
RN 112747-40-7 HCAPLUS
CN L-Threoninamide, L-tyrosyl-D-alanyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



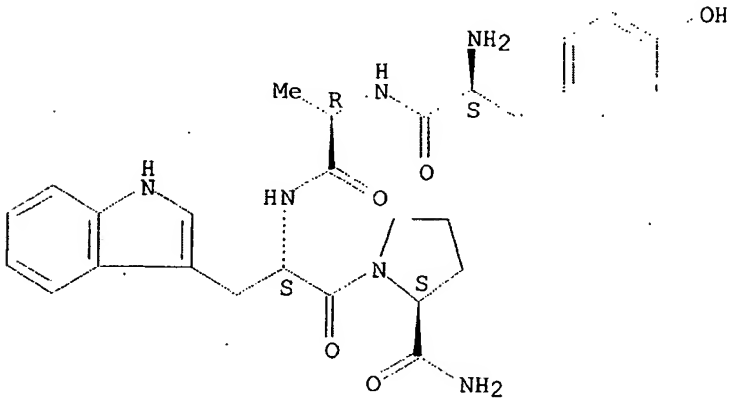
RN 112747-41-8 HCAPLUS
CN L-Proline, 1-[N-(N-L-tyrosyl-D-alanyl)-L-tryptophyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



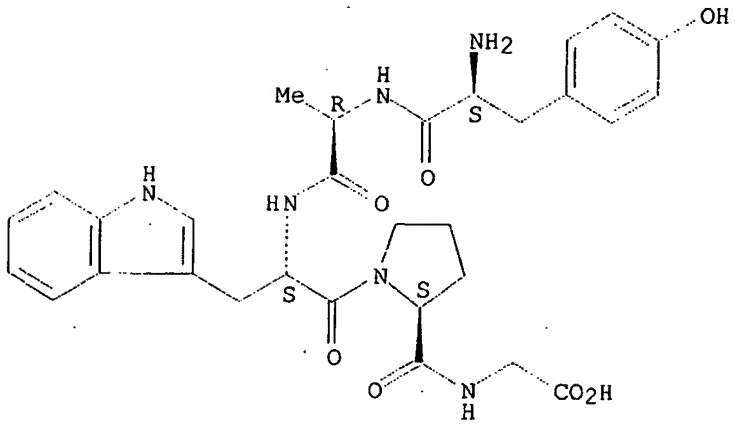
RN 112747-42-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-D-alanyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



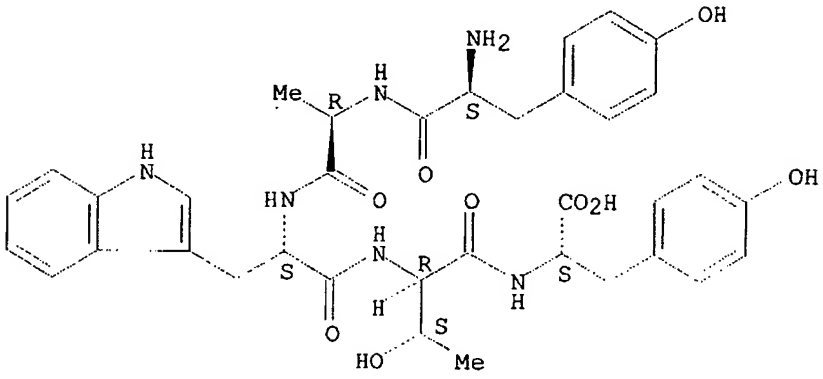
RN 112747-43-0 HCAPLUS
CN Glycine, N-[1-[N-(N-L-tyrosyl-D-alanyl)-L-tryptophyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



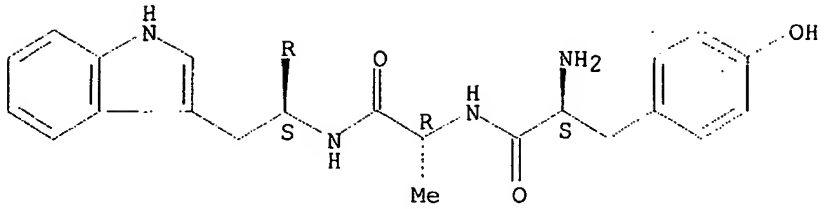
RN 112747-44-1 HCAPLUS
CN L-Tyrosine, N-[N-[N-(N-L-tyrosyl-D-alanyl)-L-tryptophyl]-D-threonyl]- (9CI) (CA INDEX NAME)

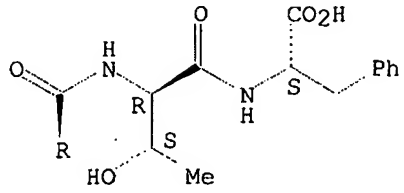
Absolute stereochemistry.



RN 112747-45-2 HCAPLUS
CN L-Phenylalanine, N-[N-[N-(N-L-tyrosyl-D-alanyl)-L-tryptophyl]-D-threonyl]- (9CI) (CA INDEX NAME)

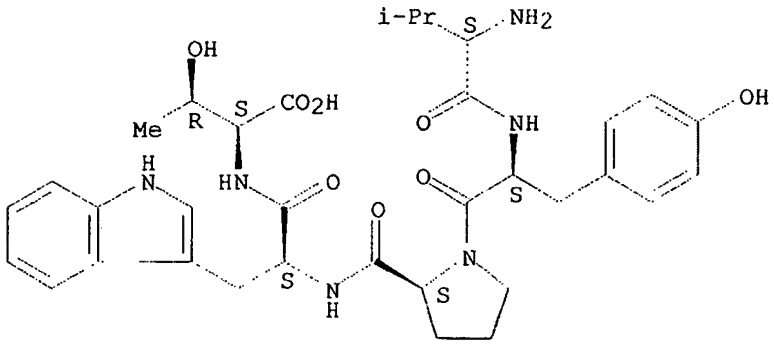
Absolute stereochemistry.





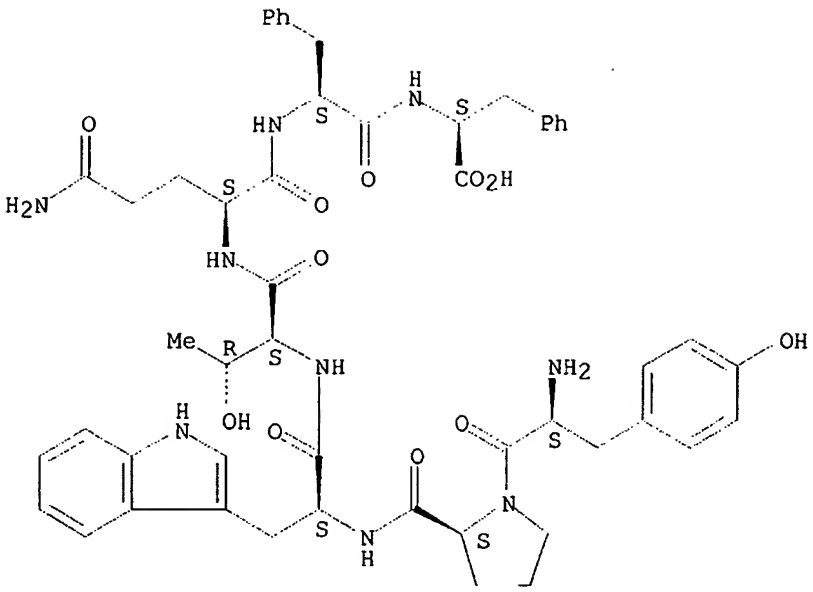
RN 112765-57-8 HCAPLUS
CN L-Threonine, L-valyl-L-tyrosyl-L-prolyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 112765-58-9 HCAPLUS
CN L-Phenylalanine, N-[N-[N2-[N-[N-(1-L-tyrosyl-L-prolyl)-L-tryptophyl]-L-threonyl]-L-glutaminyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:128613 HCAPLUS
DOCUMENT NUMBER: 104:128613
TITLE: In vitro effects of β-casomorphins on ion transport in rabbit ileum
AUTHOR(S): Hautefeuille, Matthieu; **Brantl, Victor**; Dumontier, Anne Marie; Desjeux, Jehan Francois
CORPORATE SOURCE: Unite Rech. Diabete Nutr. Chez Enfant, Inst. Natl. Sante Rech. Med., Paris, 75010, Fr.
SOURCE: American Journal of Physiology (1986), 250(1, Pt. 1), G92-G97
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of natural β-casomorphin-4-OH (Tyr-Pro-Phe-Pro-OH)(β-CM-4-OH) [**74171-19-0**], β-CM-5-OH (Tyr-Pro-Phe-Pro-Gly-OH) [**72122-63-5**], and 3 related analogs on electrolyte transport were examined in rabbit ileum in vitro. At concns. of 10-7-10-3 M, the 3 analogs β-[D-Ala2]CM-4-NH2 [**83936-20-3**], β-[D-Ala2,Met5]CM-5-NH2 [**83936-23-6**], and β-[D-Ala2,4,Tyr5]CM-5-NH2 [**100817-40-1**], caused a dose-dependent, naloxone-reversible reduction in short-circuit current (Isc) after addition to the serosal side of the preparation β-[D-Ala2,4,Tyr5]CM-5-NH2 also decreased Isc after mucosal addition Serosal addition of the same analog stimulated absorption of Na+ and Cl- (+2.90 and +2.12 μequivalent/h/cm2, resp.) and inhibited residual flux (-1.80). The natural β-casomorphins tested did not decrease Isc. Thus, β-casomorphin analogs stimulate **intestinal** absorption of electrolytes by an opioid mechanism. The fact that β-[D-Ala2,4,Tyr5]CM-5-NH2 was effective on the mucosal side favors the hypothesis that certain food-related opioid peptides might be absorbed by the **intestine**.

CC 17-13 (Food and Feed Chemistry)
ST casomorphin electrolyte absorption **intestine**
IT Electrolytes

(absorption of, by **intestine**, β-casomorphins stimulation of)

IT Receptors
RL: BIOL (Biological study)
(for opioids, β-casomorphin stimulation of electrolyte absorption by **intestine** mediation by)

IT **Intestine**, metabolism
(ileum, electrolyte absorption by, β-casomorphins stimulation of, opioid mechanism of)

IT **7440-23-5**, biological studies **16887-00-6**, biological studies
RL: BIOL (Biological study)
(absorption of, by **intestine**, β-casomorphins stimulation of)

IT **72122-63-5 74171-19-0 79805-24-6D**, analogs **83936-20-3 83936-23-6 100817-40-1**
RL: BIOL (Biological study)
(electrolyte absorption by **intestine** stimulation by, opioid mechanism of)

IT **7440-23-5**, biological studies **16887-00-6**, biological studies
RL: BIOL (Biological study)
(absorption of, by **intestine**, β-casomorphins stimulation of)

RN 7440-23-5 HCAPLUS
CN Sodium (8CI, 9CI) (CA INDEX NAME)

Na

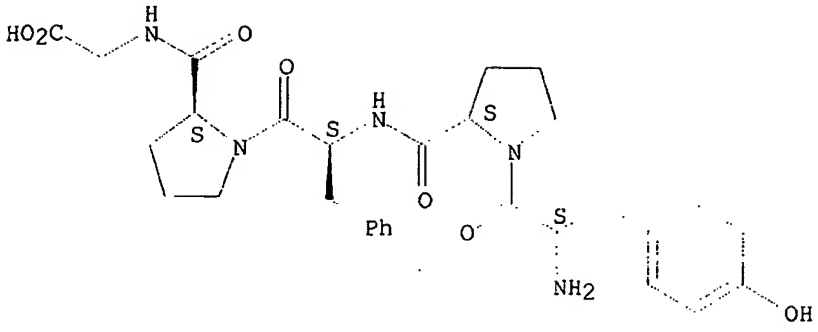
RN 16887-00-6 HCAPLUS
CN Chloride (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Cl^-

IT **72122-63-5 74171-19-0 79805-24-6D**, analogs **83936-20-3 83936-23-6 100817-40-1**
RL: BIOL (Biological study)
(electrolyte absorption by **intestine** stimulation by, opioid mechanism of)

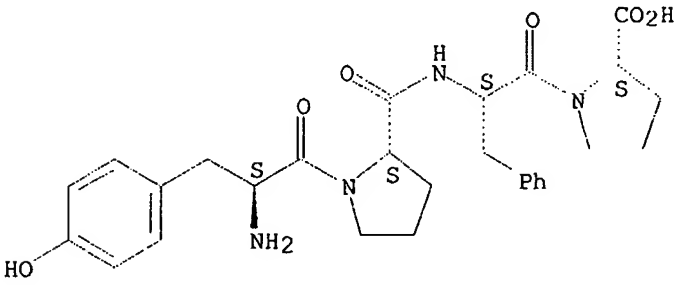
RN 72122-63-5 HCAPLUS
CN Glycine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 74171-19-0 HCAPLUS
CN L-Proline, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

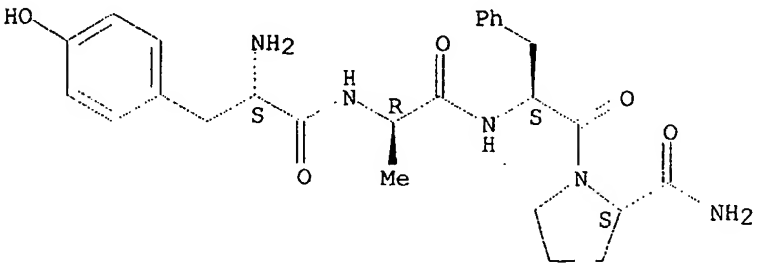
Absolute stereochemistry.



RN 79805-24-6 HCAPLUS
CN β-Casomorphin (9CI) (CA INDEX NAME)

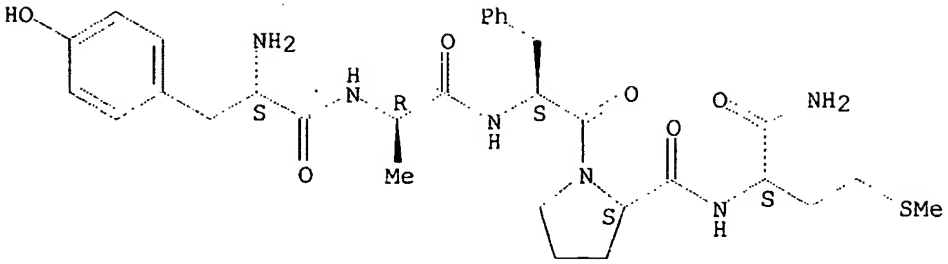
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 83936-20-3 HCAPLUS
CN L-Prolinamide, L-tyrosyl-D-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 83936-23-6 HCAPLUS
CN Dermorphin, 4-deglycine-5-de-L-tyrosine-7-L-methioninamide- (9CI) (CA INDEX NAME)

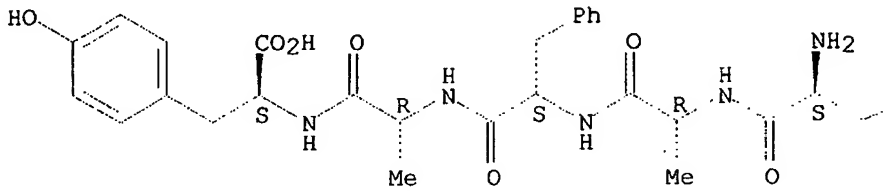
Absolute stereochemistry.



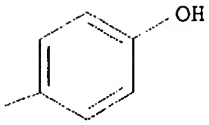
RN 100817-40-1 HCAPLUS
CN Dermorphin, 4-D-alanine-6-de-L-proline-7-de-L-serinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L28 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:572492 HCAPLUS
DOCUMENT NUMBER: 103:172492
TITLE: Effect of a β-casomorphin analog on ion transport in rabbit ileum: evidence for a cholinergic mediation
AUTHOR(S): Hautefeuille, M.; **Brantl, V.**; Dumontier, A. M.; Desjeux, J. F.
CORPORATE SOURCE: Unite Rech. Diabete Nutr. Enfant, CHU Villemin, Paris, 75010, Fr.
SOURCE: Regulatory Peptides (1985), (Suppl. 4), 219-20
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ionic transport, as measured by the short-circuit current, by rabbit ileum prepns. was inhibited by the β-casomorphin analog 4027 (Tyr-D-Ala-Phe-D-Ala-Tyr-NH2) [**98815-38-4**], and this response was prevented by the opiate antagonist naloxone. In this preparation, ionic transport was also inhibited by atropine, indicating the presence of cholinergic release. The effects of sequential addns. of 4027, naloxone, and atropine in different orders suggested that the **intestinal** ionic transport system involved an opioid receptor, a cholinergic agonist,

and an acetylcholine-sensitive epithelial layer. Evidently, 4027 suppressed a tonic cholinergic release, and the effect of 4027 was inhibited by naloxone at the opioid receptor site. Both 4027 and atropine acted at the enterocyte level.

CC 2-5 (Mammalian Hormones)

ST ileum ion transport casomorphin analog; receptor opioid ileum ion transport; cholinergic casomorphin analog ion transport ileum

IT Receptors
RL: BIOL (Biological study)
(for opiates, of ileum, in ion transport response to casomorphin analog)

IT Electrolytes
(transport of, by ileum, casomorphin ananlog inhibition of, cholinergic and opioid mechanisms for)

IT Receptors
RL: BIOL (Biological study)
(cholinergic, of **intestine** ileum, in ion transport response to casomorphin analog)

IT Opiates and Opioids
RL: BIOL (Biological study)
(endogenous, receptors for, of ileum, in ion transport response to casomorphin analog)

IT **Intestine**, metabolism
(ileum, ion transport by, casomorphin analog inhibition of, cholinergic and opioid mechanisms for)

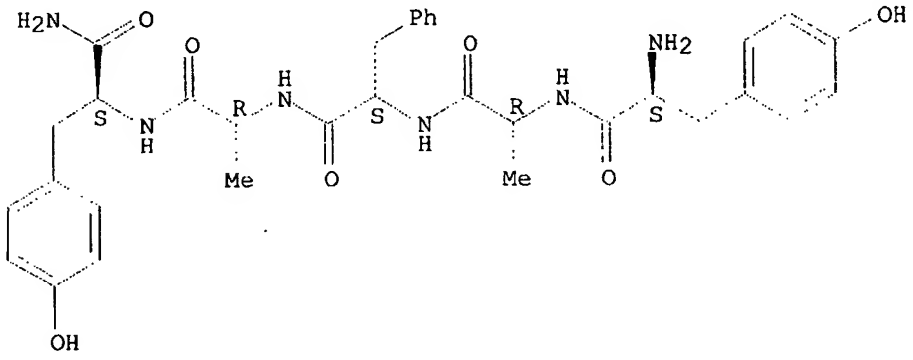
IT **98815-38-4**
RL: BIOL (Biological study)
(ion transport by ileum inhibition by, cholinergic and opioid mechanisms for)

IT **98815-38-4**
RL: BIOL (Biological study)
(ion transport by ileum inhibition by, cholinergic and opioid mechanisms for)

RN 98815-38-4 HCAPLUS

CN L-Tyrosinamide, L-tyrosyl-D-alanyl-L-phenylalanyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:482014 HCAPLUS

DOCUMENT NUMBER: 103:82014

TITLE: Novel opioid peptides derived from mitochondrial cytochrome b: cytochrophins

AUTHOR(S): **Brantl, Victor**; Gramsch, Christian; Lottspeich, Friedrich; Henschen, Agnes; Jaeger, Karl Heinz; Herz, Albert

CORPORATE SOURCE: Boehringer Ingelheim K.-G., Ingelheim, D-6507, Fed. Rep. Ger.

SOURCE: European Journal of Pharmacology (1985), 111(2), 293-4
CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The opioid activities of cytochrophin-4 (Tyr-Pro-Phe-Thr)(I) and cytochrophin-5 (Tyr-Pro-Phe-Thr-Ile) were lower than those of β-casomorphines or normorphine in the guinea pig ileum assay. The cytochrophins were isolated from Haem-Uvocal, which was obtained by treatment of bovine blood with **gastrointestinal** enzymes. I represents fragment 345-348 from mitochondrial cytochrome b.

CC 2-5 (Mammalian Hormones)

ST opioid cytochrome b fragment; cytochrophin opioid

IT Nomenclature, new natural products
(cytochrophin-4 (peptide))

IT Nomenclature, new natural products
(cytochrophin-5 (peptide))

IT Blood
(enzymic hydrolyzares, cytochrophins isolation from, opioid activity of)

IT Opiates and Opioids
RL: BIOL (Biological study)
(peptides, cytochrophins-4 and -5 as, from cytochrome b)

IT **9035-37-4D**, fragments **97730-74-0 97730-75-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opioid activity of)

IT **9035-37-4D**, fragments **97730-74-0 97730-75-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opioid activity of)

RN 9035-37-4 HCAPLUS

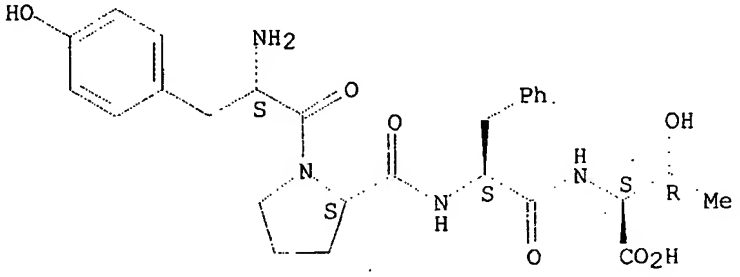
CN Cytochrome b (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 97730-74-0 HCAPLUS

CN L-Threonine, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

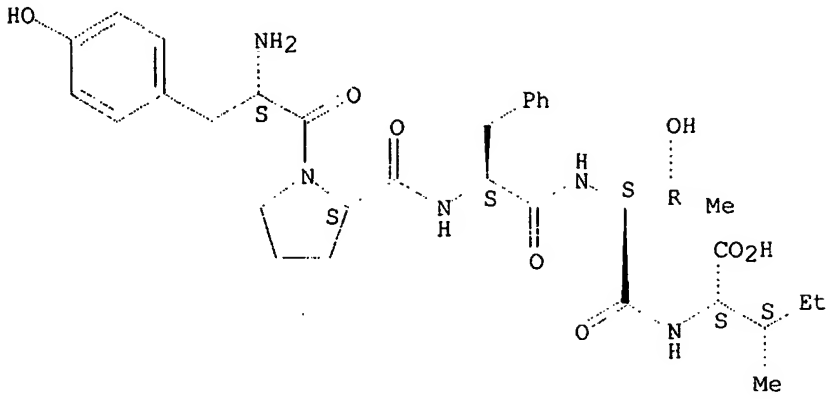
Absolute stereochemistry.



RN 97730-75-1 HCAPLUS

CN L-Isoleucine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

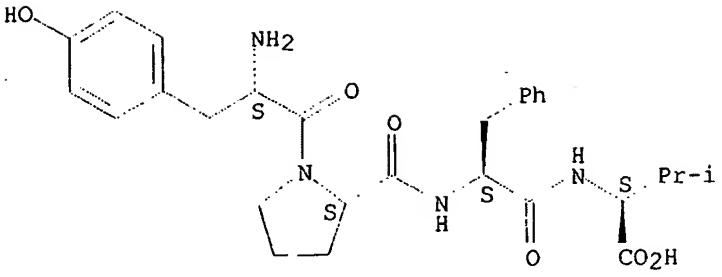


L28 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:110584 HCAPLUS
DOCUMENT NUMBER: 102:110584
TITLE: Novel opioid peptides derived from human β-casein: human β-casomorphins
AUTHOR(S): **Brantl, Victor**
CORPORATE SOURCE: Dep. Med., Boehringer Ingelheim K.-G., Ingelheim am Rhein, D-6507, Fed. Rep. Ger.
SOURCE: European Journal of Pharmacology (1984), 106(1), 213-14
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human β-casomorphins 4 (Tyr-Pro-Phe-Val) and 5 (Tyr-Pro-Phe-Val-Glu) were less potent than the corresponding bovine β-casomorphin 4 (Tyr-Pro-Phe-Pro) and 5 (Tyr-Pro-Phe-Pro-Gly) in inhibiting the contraction of the guinea pig ileum induced by elec. stimulation.

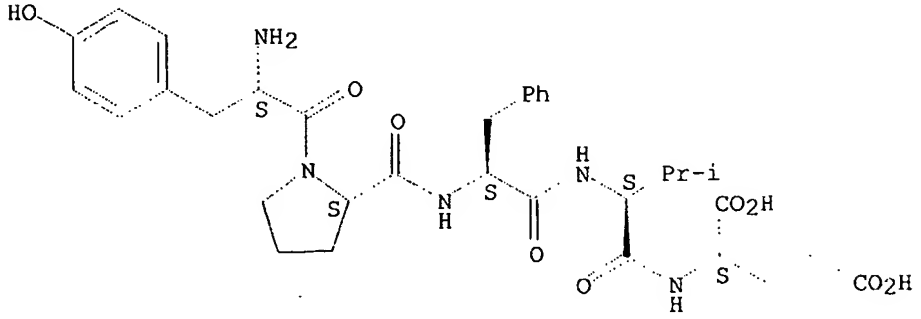
CC 13-6 (Mammalian Biochemistry)
ST casomorphin ileum contraction
IT **Intestine**
(ileum, contraction of, β-casomorphins 4 and 5 of human inhibition of)
IT Muscle
(smooth, contraction of, β-casomorphins 4 and 5 of human inhibition of)
IT **94664-03-6 94664-04-7**
RL: BIOL (Biological study)
(ileum contraction inhibition by)
IT **94664-03-6 94664-04-7**
RL: BIOL (Biological study)
(ileum contraction inhibition by)
RN 94664-03-6 HCAPLUS
CN L-Valine, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 94664-04-7 HCAPLUS
CN L-Glutamic acid, L-tyrosyl-L-prolyl-L-phenylalanyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:540411 HCAPLUS
DOCUMENT NUMBER: 99:140411
TITLE: Pharmacologically active peptides and medicaments containing them
INVENTOR(S): **Brantl, Victor**; Henschen, Agnes; Teschemacher, Hansjoerg; Lottspeich, Friedrich
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 229,577. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

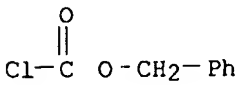
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4390527	A	19830628	US 1981-258617	19810429
DE 2936099	A1	19810402	DE 1979-2936099	19790906
BR 8008818	A	19810623	BR 1980-8818	19800904
JP 56501648	T2	19811112	JP 1980-502020	19800904
JP 03069920	B4	19911105		
US 4681871	A	19870721	US 1981-229577	19810122
DK 8101998	A	19810505	DK 1981-1998	19810505
DK 160316	B	19910225		
DK 160316	C	19910729		

US 4555403 A 19851126 US 1983-507807 19830624
PRIORITY APPLN. INFO.: DE 1979-2936099 19790906
US 1981-229577 19810122
DE 1979-2921216 19790525
WO 1980-DE72 19800520
WO 1980-DE126 19800904
US 1981-258617 19810429

AB β-Casomorphin tri- to nonapeptide analogs from H-Tyr-X-X1-OH to H-Tyr-X-X1-Pro-X2-Pro-Leu-Pro-X3-OH (X = D-Pro, D-Ala, D-Thr, D-Val; X1 = Phe, Pro, Tyr; X2 = Gly, Pro, Tyr; X3 = Asn, Pro, Ile) were prepared as opiates. Thus, H-Tyr-X4-Phe-Pro-Gly-OMe (X4 = D-Ala, D-Pro) were prepared by conventional solution methods using mixed anhydride peptide coupling reactions. D-Ala2-β-casomorphin exhibited opiate activity in the guinea pig **intestine** test after 120 min exposure to enzymes, whereas β-casomorphin was inactive after 30 min.

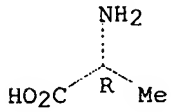
IC A61K037-00; C07C103-52
NCL 424177000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63
ST casomorphin analog prepn opiate
IT Opiates and Opioids
RL: RCT (Reactant); RACT (Reactant or reagent)
(β-casomorphin analogs)
IT **501-53-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzyloxycarbonylation by, of D-alanine)
IT **338-69-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzyloxycarbonylation of)
IT **5680-79-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with dipeptide derivative)
IT **7669-64-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with glycine Me ester)
IT **29713-96-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with tetrapeptide Me esters)
IT **6404-31-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with tripeptide Me ester)
IT **77434-40-3P 79706-54-0P 79706-55-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
IT **79805-24-6DP**, analogs
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and opiate activity of)
IT **26607-51-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with tripeptide Me ester)
IT **79706-56-2P 79706-57-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with tyrosine derivative)
IT **77434-41-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with D-alanine or D-proline derivative)

IT **79706-52-8P 79706-53-9P 82289-40-5P**
83936-22-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **501-53-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzyloxycarbonylation by, of D-alanine)
RN 501-53-1 HCAPLUS
CN Carbonochloridic acid, phenylmethyl ester (9CI) (CA INDEX NAME)

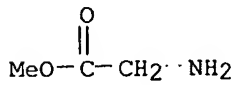


IT **338-69-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzyloxycarbonylation of)
RN 338-69-2 HCAPLUS
CN D-Alanine (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

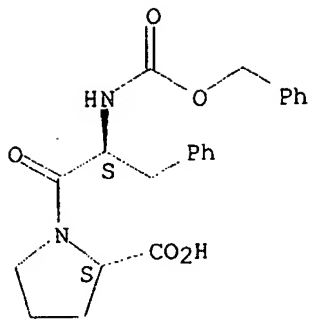


IT **5680-79-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with dipeptide derivative)
RN 5680-79-5 HCAPLUS
CN Glycine, methyl ester, hydrochloride (6CI, 8CI, 9CI) (CA INDEX NAME)



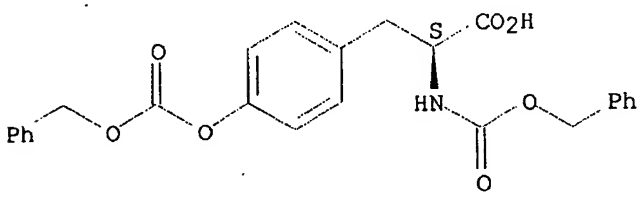
IT **7669-64-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with glycine Me ester)
RN 7669-64-9 HCAPLUS
CN L-Proline, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



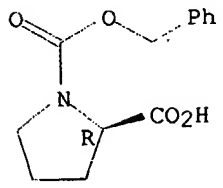
IT **29713-96-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with tetrapeptide Me esters)
RN 29713-96-0 HCAPLUS
CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-, phenylmethyl carbonate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



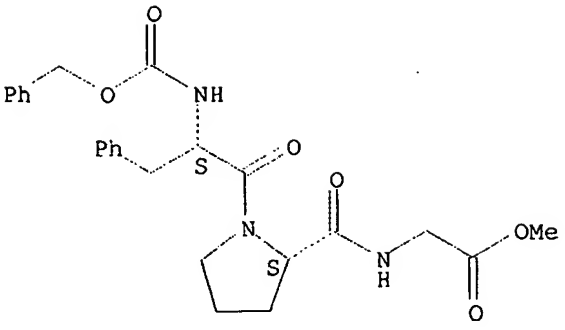
IT **6404-31-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with tripeptide Me ester)
RN 6404-31-5 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 1-(phenylmethyl) ester, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



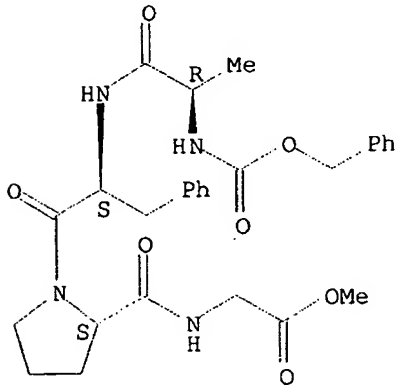
IT **77434-40-3P 79706-54-0P 79706-55-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
RN 77434-40-3 HCAPLUS
CN Glycine, N-[1-[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



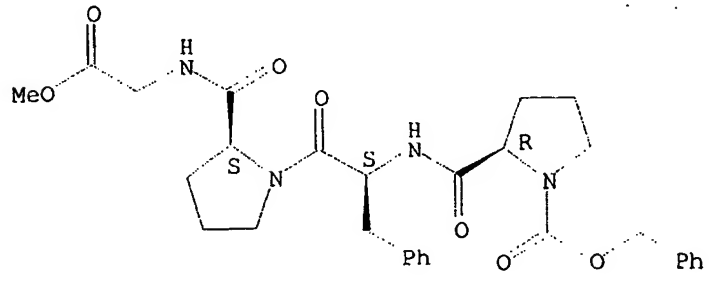
RN 79706-54-0 HCAPLUS
CN Glycine, N-[1-[N-[N-[(phenylmethoxy)carbonyl]-D-alanyl]-L-phenylalanyl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 79706-55-1 HCAPLUS
CN Glycine, N-[1-[N-[1-[(phenylmethoxy)carbonyl]-D-prolyl]-L-phenylalanyl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

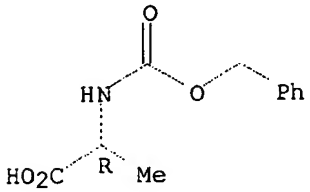


IT **79805-24-6DP**, analogs
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and opiate activity of)

RN 79805-24-6 HCAPLUS
CN β-Casomorphin (9CI) (CA INDEX NAME)

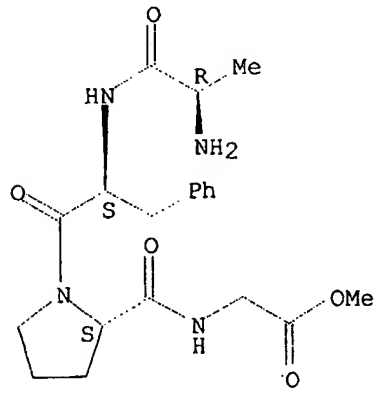
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **26607-51-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with tripeptide Me ester)
RN 26607-51-2 HCAPLUS
CN D-Alanine, N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



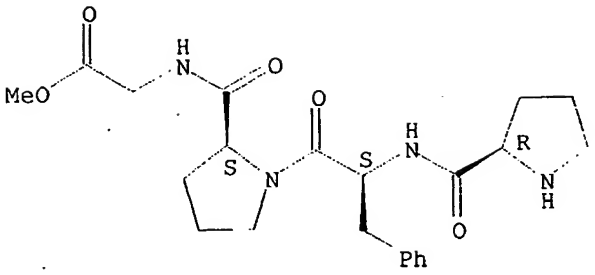
IT **79706-56-2P 79706-57-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with tyrosine derivative)
RN 79706-56-2 HCAPLUS
CN Glycine, N-[1-(N-D-alanyl-L-phenylalanyl)-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



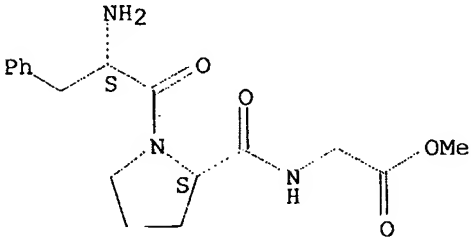
RN 79706-57-3 HCAPLUS
CN Glycine, N-[1-(N-D-prolyl-L-phenylalanyl)-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



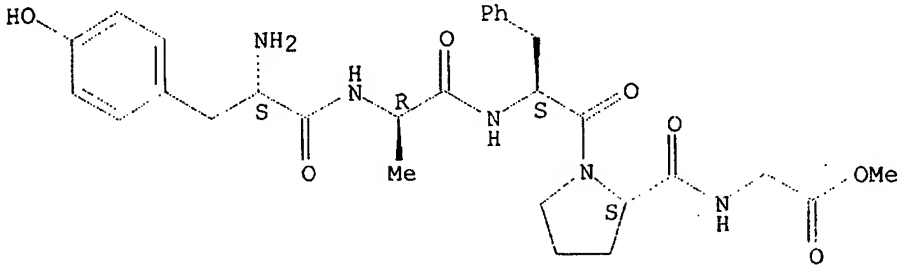
IT **77434-41-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with D-alanine or D-proline derivative)
RN 77434-41-4 HCAPLUS
CN Glycine, L-phenylalanyl-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



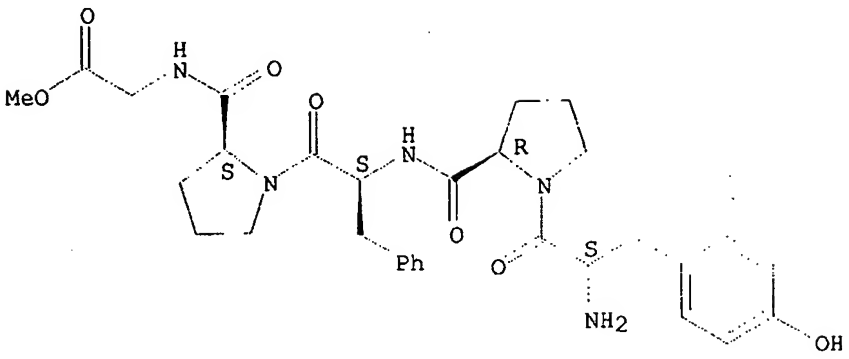
IT **79706-52-8P 79706-53-9P 82289-40-5P**
83936-22-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 79706-52-8 HCAPLUS
CN Glycine, N-[1-[N-(N-L-tyrosyl-D-alanyl)-L-phenylalanyl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



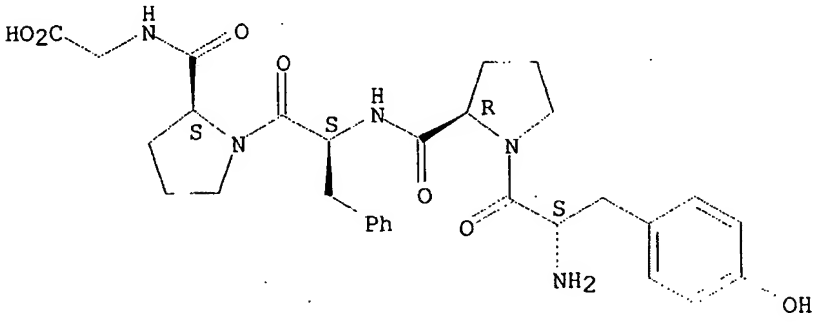
RN 79706-53-9 HCAPLUS
CN Glycine, N-[1-[N-(1-L-tyrosyl-D-prolyl)-L-phenylalanyl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



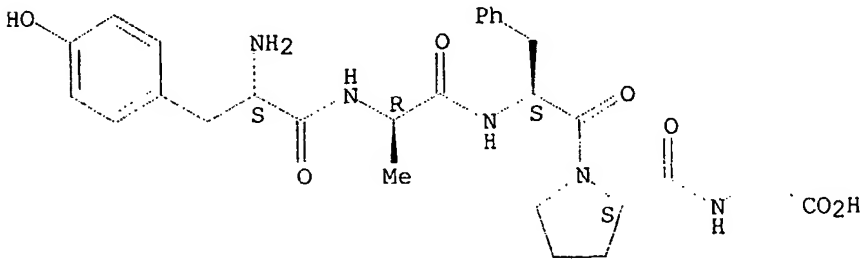
RN 82289-40-5 HCAPLUS
CN Glycine, N-[1-[N-(1-L-tyrosyl-D-prolyl)-L-phenylalanyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 83936-22-5 HCAPLUS
CN Dermorphin, 4-deglycine-5-de-L-tyrosine-7-glycine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:416934 HCAPLUS
DOCUMENT NUMBER: 99:16934
TITLE: Effect of β-casomorphins on somatostatin release

in dogs

AUTHOR(S): Schusdziarra, V.; Schick, R.; De la Fuente, A.; Holland, A.; **Brantl, V.**; Pfeiffer, E. F.

CORPORATE SOURCE: Dep. Int. Med. I, Univ. Ulm, Ulm, Fed. Rep. Ger.

SOURCE: Endocrinology (1983), 112(6), 1948-51
CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of orally administered β-casomorphins (β-CM) and methionine-enkephalin (met-enkephalin) [**58569-55-4**] on postprandial plasma somatostatin [**51110-01-1**]-like immunoreactivity (SLI) were assessed in conscious dogs. The intragrastic instillation of a liver extract-sucrose test meal containing 12 mg β-CM or 10 mg met-enkephalin, resp., augmented the postprandial rise of peripheral vein plasma SLI levels. This effect was inhibited by the addnl. administration of the specific opiate-receptor antagonist, naloxone. When liver extract and sucrose was dissolved in fresh bovine milk the increase of plasma SLI levels was greater than liver extract and sucrose dissolved in water. This milk-induced augmentation of SLI levels was also reduced by naloxone. Since these opiate-active compds. have and influence on insulin release when given i.v., the effect of β-CM-7 [**72122-62-4**], β-CM-5 [**72122-63-5**], β-CM-4 [**74171-19-0**], β-CM-4-amide [**74135-04-9**], and met-enkephalin on SLI levels was assessed during i.v. infusion at a rate of 1 nmol/kg/h during an i.v. background infusion of a glucose-amino acid mixture The infusion of β-CM-5 increased peripheral vein SLI levels, whereas the infusion of met-enkephalin decreased SLI levels. β-CM-7, β-CM-4, and β-CM-4-amide had no effect on plasma SLI levels at the dose employed. Thus, in dogs, the ingestion of opiate-active peptide stimulates postprandial SLI release, indicating that nutrient-contained opiate-active material (exorphins) might participate in the regulation of postprandial **gastrointestinal** endocrine function.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 18

ST casomorphin somatostatin plasma; enkephalin somatostatin plasma

IT Opiates and Opioids
RL: BIOL (Biological study)
(somatostatin of blood plasma response to dietary)

IT Blood plasma
(somatostatin of, β-casomorphins and enkephalin dietary administration effect on)

IT **51110-01-1**
RL: BIOL (Biological study)
(of blood plasma, β-casomorphins and enkephalin dietary administration effect on)

IT **72122-62-4 72122-63-5 74135-04-9**
74171-19-0
RL: BIOL (Biological study)
(somatostatin of blood plasma response to dietary)

IT **58569-55-4**
RL: BIOL (Biological study)
(somatostatin of blood plasma response to dietary, β-casomorphins in relation to)

IT **51110-01-1**
RL: BIOL (Biological study)
(of blood plasma, β-casomorphins and enkephalin dietary administration effect on)

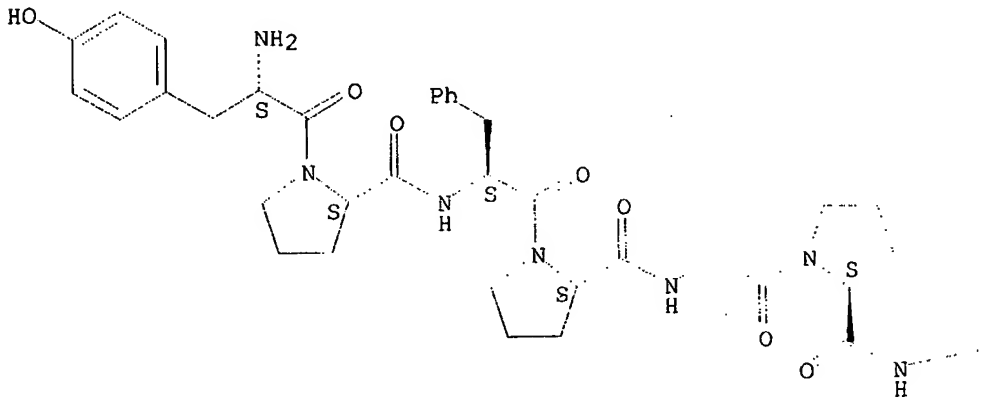
RN 51110-01-1 HCAPLUS

CN Somatostatin (9CI) (CA INDEX NAME)

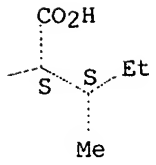
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **72122-62-4 72122-63-5 74135-04-9**
74171-19-0
RL: BIOL (Biological study)
(somatostatin of blood plasma response to dietary)
RN 72122-62-4 HCAPLUS
CN L-Isoleucine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

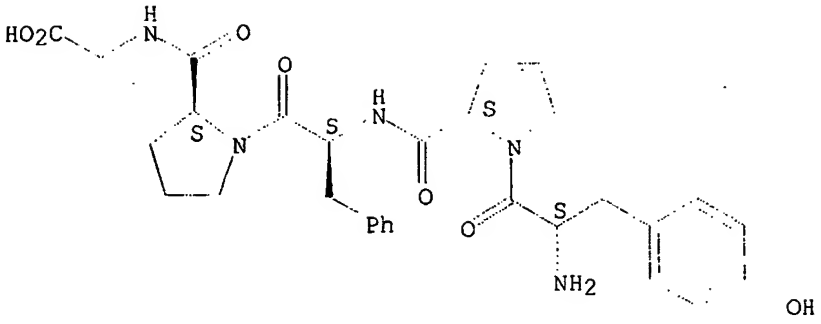


PAGE 1-B



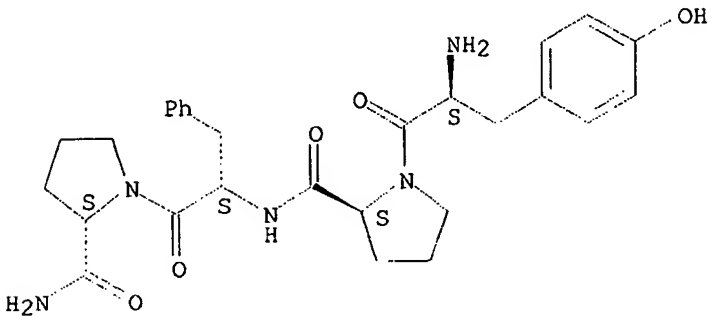
RN 72122-63-5 HCAPLUS
CN Glycine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



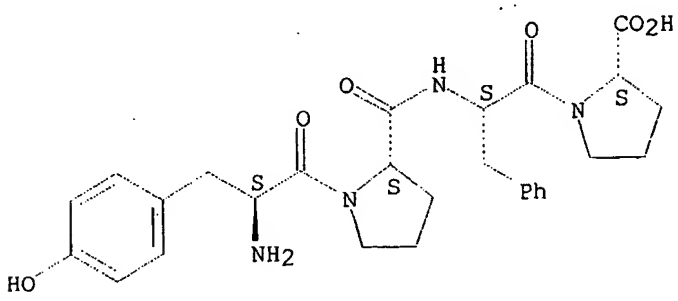
RN 74135-04-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 74171-19-0 HCAPLUS
CN L-Proline, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

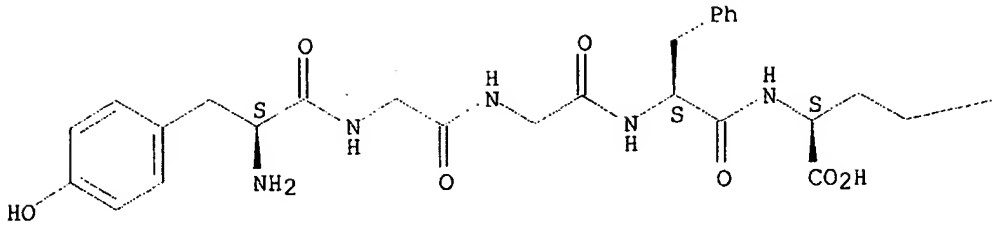
Absolute stereochemistry.



IT **58569-55-4**
RL: BIOL (Biological study)
(somatostatin of blood plasma response to dietary, β-casomorphins in relation to)
RN 58569-55-4 HCAPLUS
CN 1-5-Adrenorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—SMe

L28 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:484549 HCAPLUS
DOCUMENT NUMBER: 97:84549
TITLE: Isolation of pharmacologically active peptides by high-pressure liquid chromatography (HPLC)
AUTHOR(S): **Brantl, Victor**
CORPORATE SOURCE: Abt. Neuropharmakol., Max-Planck-Inst. Psychiatrie, Munich, D-8000/40, Fed. Rep. Ger.
SOURCE: High Perform. Liq. Chromatogr. Protein Pept. Chem., Proc. Int. Symp. (1981), 365-84. Editor(s): Lottspeich, Friedrich; Henschen, Agnes; Hupe, Klaus-Peter. de Gruyter: Berlin, Fed. Rep. Ger. CODEN: 48BDAM
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A material which displayed opioid activity in the guinea pig ileum longitudinal muscle-myenteric plexus preparation was extracted from an enzymic bovine casein digest into CHCl3-MeOH. The extract was roughly purified by absorption/desorption procedures by use of charcoal and Amberlite XAD 2 resin as adsorbents. The material was then submitted to 5 HPLC purification steps on μBondapak C18 and μPorasil. In the last step, a single compound was obtained which contained a pure heptapeptide with the sequence Tyr-Pro-Phe-Pro-Gly-Pro-Ile. This opioid peptide, which is highly resistant towards proteolytic enzymes, was a fragment of bovine β-casein. In view of its origin from β-casein and its opiate activity, this peptide was named β-casomorphin-7 [**72122-62-4**]. Detailed information concerning the purification procedures, the purity criteria, structure anal., and some pharmacol. properties of β-casomorphin-7 and its smaller fragments are described.

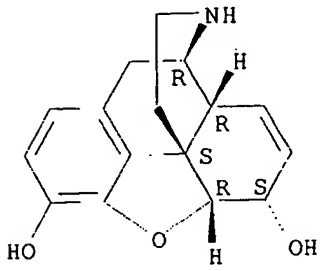
CC 1-1 (Pharmacology)
ST opioid high pressure liq chromatog; ileum opioid peptide purifn
IT Enkephalins
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of, of guinea pig ileum by high-performance liquid chromatog.)
IT Chromatography, column and liquid
(high-pressure, of opioid peptides)
IT **Intestine**, composition
(ileum, opioids purification in, of guine pig by high-performance liquid chromatog.)
IT **466-97-7P 58569-55-4P 72122-62-4P**

72122-63-5P 74171-19-0P 77434-43-6P
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of, of guinea pig ileum by high-performance liquid chromatog.)

IT **466-97-7P 58569-55-4P 72122-62-4P**
72122-63-5P 74171-19-0P 77434-43-6P
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of, of guinea pig ileum by high-performance liquid chromatog.)

RN 466-97-7 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-, (5α,6α)- (9CI)
(CA INDEX NAME)

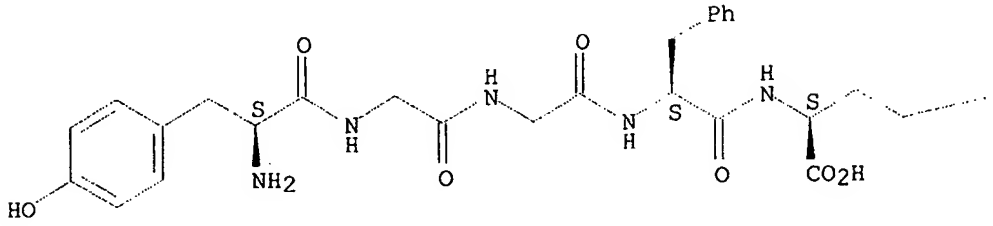
Absolute stereochemistry.



RN 58569-55-4 HCAPLUS
CN 1-5-Adrenorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



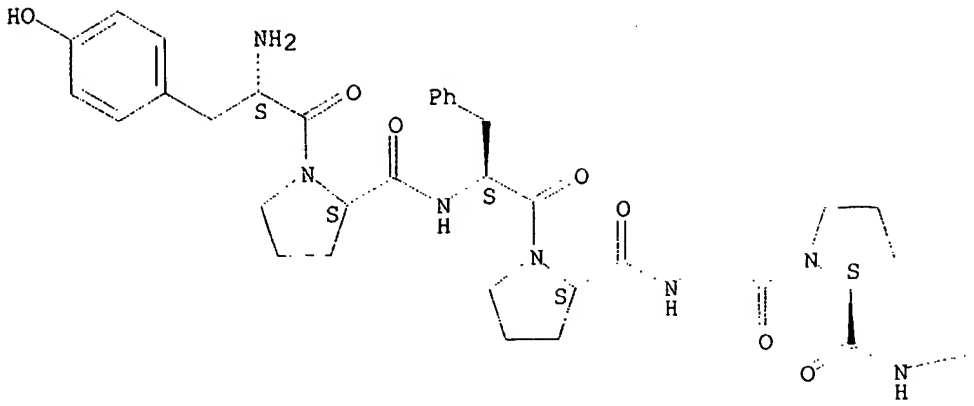
PAGE 1-B

—SMe

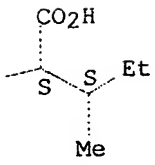
RN 72122-62-4 HCAPLUS
CN L-Isoleucine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolylglycyl-L-prolyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

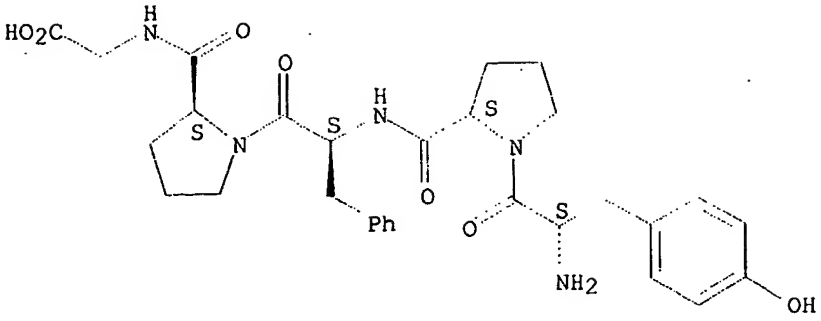


PAGE 1-B



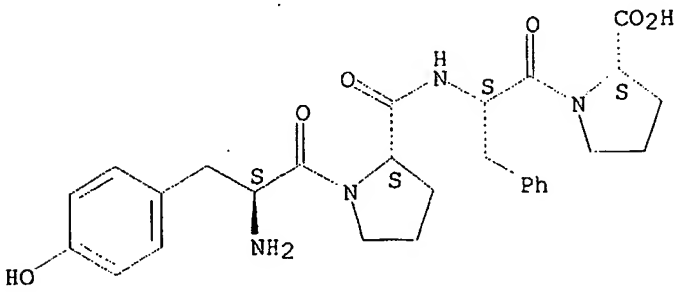
RN 72122-63-5 HCAPLUS
CN Glycine, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 74171-19-0 HCAPLUS
CN L-Proline, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 77434-43-6 HCAPLUS
CN L-Proline, L-tyrosyl-L-prolyl-L-phenylalanyl-L-prolylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.